1,5-Bifunctional Organomagnesium Reagents for the Direct Transformation of Esters into Arenes

Inauguraldissertation

zur

Erlangung der Würde eines Doktors der Philosophie

vorgelegt der

Philosophisch-Naturwissenschaftlichen Fakultät

der Universität Basel

von

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Deutschland

Basel, 2018

Genehmigt von der Philosophisch-Naturwissenschaftlichen Fakultät
auf Antrag von

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Basel, den 27.03.2018

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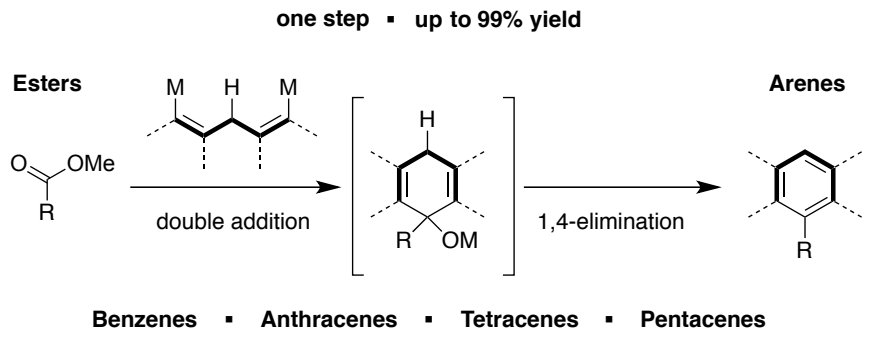
Abstract

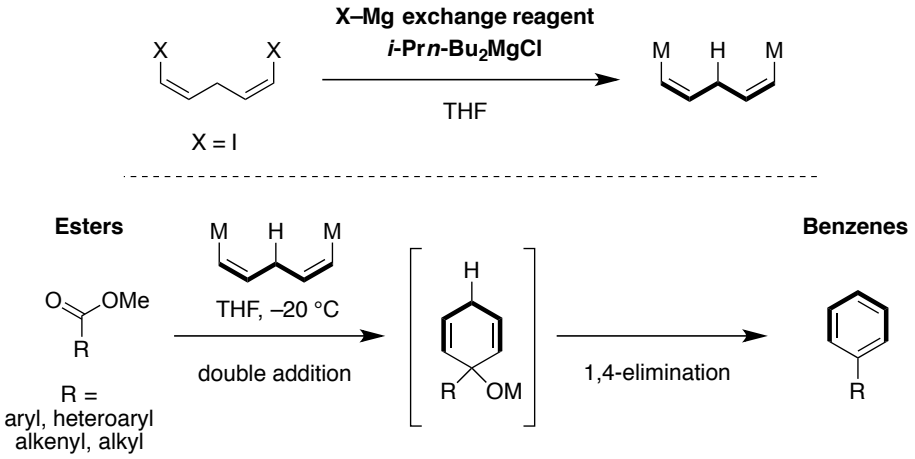
For the sustainable and economical supply of products relevant to our society, the development of new methods based on main group elements is indispensable. Arenes are privileged molecular scaffolds due to their stability, rigidity and their manifold use in functional or bioactive entities. Nowadays, transition metal catalyzed cross-coupling reactions are the most frequently employed and efficient methods to functionalize arenes by means of C–C-bond formation. However, they require prefunctionalized coupling partners and remaining catalyst impurities are difficult to be removed to the required levels. Thus, transition-metal-free methods to synthesize substituted arenes from readily available starting materials are highly desirable. Carboxylic acid ester are ubiquitous intermediates in organic synthesis and are therefore the ideal substrates for the synthesis of arene derivatives.

In this thesis the development of a one step transformation of carboxylic acid esters into substituted arenes with 1,5-bifunctional organomagnesium reagents is described. The Grignard reagents react with the esters in a twofold nucleophilic addition, which is followed by an ensuing 1,4-elimination, incorporating the carboxylic carbon-atom into the newly formed aromatic ring. Various arene derivatives like substituted benzenes and polycyclic aromatic hydrocarbons like anthracenes, tetracenes and pentacenes were synthesized in yields up to 99%.

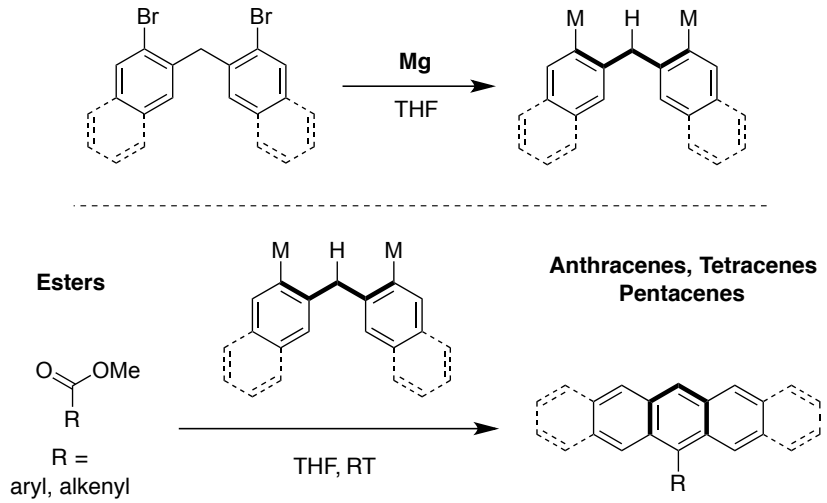


The remarkable advancement of mild halogen-magnesium exchange reactions over the recent years allowed to access a 1,5-dimagnesium-1,4-pentadiene reagent from the corresponding diiodo-precursor. The reagent was utilized to efficiently convert esters into substituted benzene. Various derivatives such as

aryl-, heteroaryl-, alkenyl- and alkyl-substituted benzenes were prepared in yields up to 82% by this direct [5+1]-benzene-forming reaction under mild conditions.

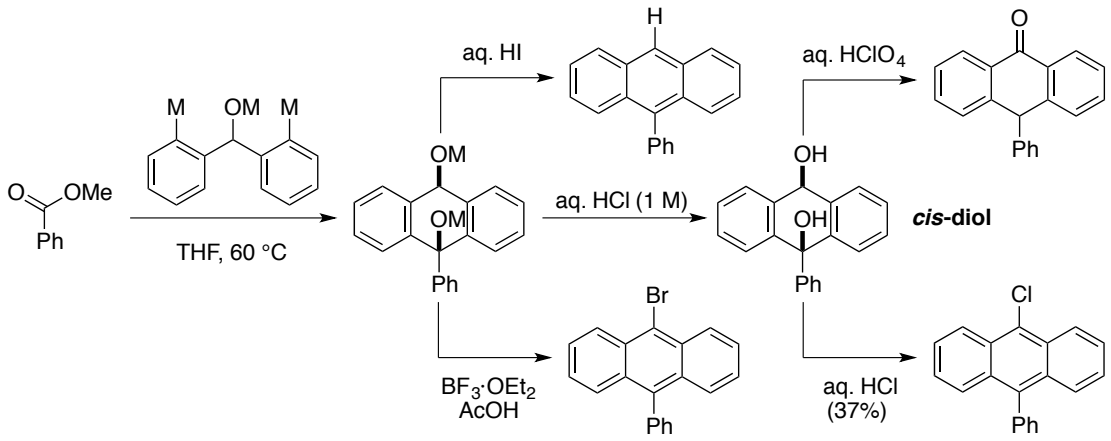


The corresponding 1,5-bifunctional bifunctional arylic organomagnesium reagents were obtained by the direct oxidative addition of elemental magnesium into the Ar–Br-bond of *o,o*'-dibromoarylmethanes. These reagents show a higher stability in comparison to the pentadiene-Grignard reagent and react with esters at room temperature with extraordinary efficiency. Even mono-substituted pentacenes, sensitive to light and oxygen can be successfully prepared by this mild method in yields up to 97%.

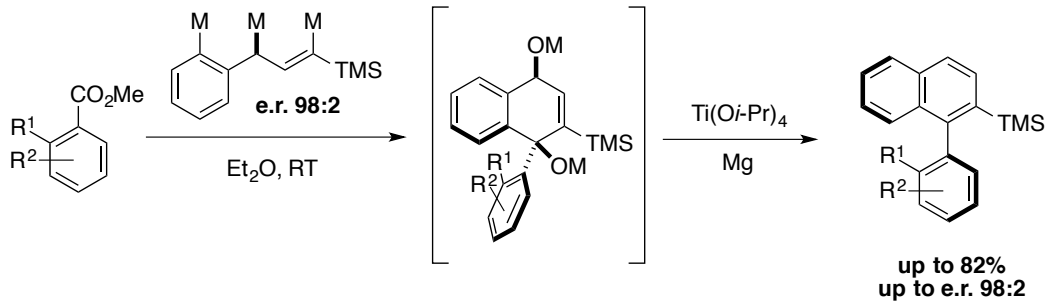


An organomagnesium alkoxide reagent prepared by a deprotonation-magnesiation sequence from readily available bis(2-bromophenyl)methanol allowed the synthesis of disubstituted anthracenes and anthrones. Halogen-

substituted and reduced derivatives were obtained by variation of the workup conditions in one synthetic step. Workup with aq. HCl (1M) allowed to isolate the corresponding *cis*-diol in excellent yield. Remarkably, a high level of diastereoselectivity was observed, which presumably is a result of coordination of the alkoxide metal to the ester carboxyl oxygen in the second addition step.



Based on this observation, the preparation of a chiral 1,5-bifunctional organomagnesium alkoxide reagent derived from a chiral propargylic alcohol was developed. This allowed to implement a stereoselective direct ester to naphthalene transformation by means of central to axial chirality conversion giving direct access to valuable axially chiral TMS-substituted naphthalenes.



Full stereospecificity was observed with substrates with sufficient substitution. Moreover, products with low rotational barriers could be efficiently prepared under the mild reaction conditions with good stereoselectivity. Intriguingly, complete reversal of the stereoselectivity was observed in the transformation of a unprotected deprotonated indole-ester.

Publications

Parts of this Ph.D thesis have been published.

- **Direct Transformation of Esters into Arenes with 1,5-Bifunctional Organomagnesium Reagents**
  A. Link, C. Fischer, C. Sparr*
  Angew. Chem. **2015**, *127*, 12331–12334; *Angew. Chem. Int. Ed.* **2015**, *54*, 12163–12166.
  http://dx.doi.org/10.1002/anie.201505414
  Highlighted in *Synfacts* **2015**, 12163.

- **A 1,5-Bifunctional Organomagnesium Reagent for the Synthesis of Disubstituted Anthracenes and Anthrones**
  A. Link, C. Fischer, C. Sparr*
  Synthesis **2017**, *49*, 397–402.
  http://dx.doi.org/10.1055/s-0036-1588087

- **Tutorial Review: Stereoselective Arene Formation**
  A. Link, C. Sparr*
  Chem. Soc. Rev. **2018**, *47*, 3804–3815.
  http://dx.doi.org/10.1039/c7cs00875a

- **Remote Central-to-Axial Chirality Conversion: Direct Atroposelective Ester to Biaryl Transformation**
  A. Link, C. Sparr*
  Angew. Chem. **2018**, *130*, 7254–7257; *Angew. Chem. Int. Ed.* **2018**, *57*, 7136–7139.
  http://dx.doi.org/10.1002/anie.201803472

Table of Contents

List of Abbreviations

$[\alpha]_D^T$	specific rotation sodium D line at temperature T
°C	degrees centigrade
®	registered trade mark
acac	acetylacetonate
AcOH	acetic acid
add.	addition
aq.	aqueous
Ar	aryl
ATR-IR	attenuated total reflection IR
Bu	butyl
calcd.	calculated
CAM	cerium ammonium molybdate stain
cat	catalytic
CCDC	Cambridge Crystallographic Data Centre
cf.	latin confer "compare"
cis	relative stereodescriptor: same side of a plane
cod	cycloocta-1,5-diene
d.r.	diastereomeric ratio
dba	dibenzylideneacetone
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
decomp.	decomposition
deion.	deionized
DIBALH	diisobutylaluminium hydride
DMF	dimethylformamide
DOSY	diffusion-ordered spectroscopy
(*E*)-	absolute stereodescriptor ("entgegen")
e.g.	latin exempli gratia "for example"
e.r.	enantiomeric ratio
ee	enantiomeric excess
eq.	equivalent
ESI-MS	electrospray ionization mass spectrometry
Et	ethyl
EtOAc	ethyl acetate
EXAFS	extended X-ray absorption fine structure
FT-IR	Fourier-transform infrared spectroscopy
ΔG	Gibbs energy difference
GC-MS	gaschromatography-mass spectrometry
gem	geminal
h	hour(s)
HPLC	High Performance Liquid Chromatography
HR-MS	High-resolution mass spectrometry
i-Pr	*iso*-propyl
i.e.	latin id est "that is"
IR	infrared spectroscopy
K	Kelvin
L	Ligand
LDA	lithium diisopropylamide
m-	*meta*-
Me	methyl
Mg*	Rieke magnesium
MHz	mega hertz
min	minute(s)
MS	mass spectrometry
Ms	methanesulfonyl
MTBE	methyl *tert*-butyl ether
n-Bu	*n*-butyl (linear chain)
NBS	N-bromosuccinimide
NFSI	N-fluorodibenzenesulfonimide
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
o-	*ortho*-
p-	*para*-
pH	potential of hydrogen
Ph	phenyl
Pin	pinacol group
prim	primary
R	residue

(*R*)-	stereodescriptor *rectus* = right handed
(R_a)-	stereodescriptor axial chirality (right handed)
rac	racemic
Red-Al®	sodium bis(2methoxy-ethoxy)aluminium hydride
R_f	retention factor
RT	room temperature
(*S*)-	stereodescriptor *sinister* = left handed
(S_a)-	stereodescriptor axial chirality (left handed)
sat.	saturated
sec-	secondary
SET	single electron transfer
S_N2	nucleophilic substitution 2nd order
T	temperature
t	time
TBAB	tetra-*n*-butylammonium bromide
TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethane-sulfonyl
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TM	unregistered trade mark
TMEDA	*N*,*N*,*N*'*N*'-tetramethyl-ethan-1,2-diamin
TMP	2,2,6,6-tetramethyl-piperidine
TMS	trimethylsilyl
t_R	retention time
trans-	relative stereodescriptor: opposite side of a plane
TS	transition state
Ts	4-toluenesulfonyl
UV	ultraviolet
(*Z*)-	absolute stereodescriptor for alkenes ("zusammen")

1 Introduction

1.1 Grignard Reagents

1.1.1 Overview

Main group organometallic reagents are an indispensable part of organic chemistry and are frequently applied in transmetalation reactions or as nucleophiles to form carbon-carbon bonds and carbon-heteroatom bonds.[1] In contrast to costly transition metals like Pd, Rh and Ru, which are mainly used as catalysts in cross-couplings or metathesis reactions, main group organometallic reagents are typically employed in stoichiometric amounts.[2] The reactivity trends of organometallic reagents are generally displayed by the electronegativity differences between the metals i.e. depend on the polarization of the carbon-metal bond.

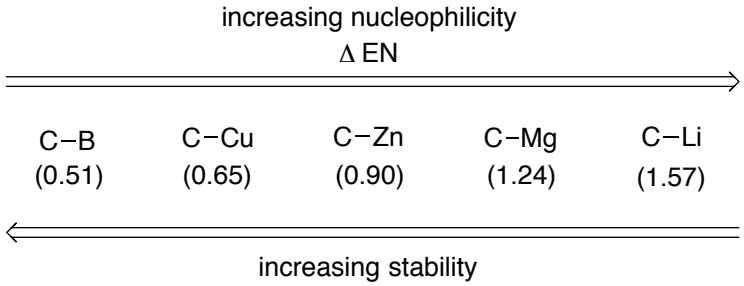
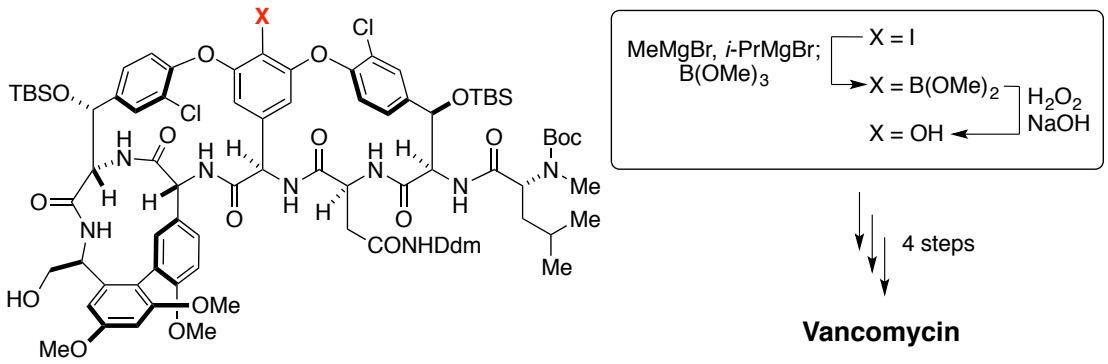


Figure 1: Simplified illustration of the reactivity trends of organometallic reagents. Substituents are neglected. The electronegativity differences (Pauling scale) between carbon and the metals in brackets.

Organoboron reagents have a low reactivity towards electrophiles, which is in stark contrast to lithium-organyls that are highly reactive and thus characterized by a limited functional group tolerance even at cryogenic temperatures.[3] Magnesium-organyls have a balanced reactivity and are usually the preferred main group organometallic reagents.[4] They show a sufficient reactivity to attack a broad range of electrophiles, but tolerate various functional groups depending on controllable conditions like temperature and solvent. The advent of modern halogen–magnesium exchange reagents allows to circumvent drawbacks associated with the use of elemental magnesium for the preparation of Grignard reagents and enable to individually tune their reactivity for the desired reaction.[5] Furthermore, these new reagents offer the opportunity to develop efficient continuous flow chemistry.[6] In situ transmetalations, as well as the combination of Grignard reagents with transition metal catalysts broaden the scope of

applicable electrophiles dramatically and make cross coupling reactions feasible.[7] While Grignard reagents have to be usually prepared in situ and converted in an inert atmosphere, their low toxicity and price makes them probably to one of the most employed in the organometallic reagent family. Moreover, many of the most important reagents have become commercially available as THF or Et_2O solutions over the recent years. Organomagnesium reagents are broadly utilized in research laboratories for the synthesis of various bioactive and functional compounds important for our society.[8]

A suitable example demonstrating the notable mildness of halogen-magnesium exchange reactions is a late-stage functionalization in K.C. Nicolaou's total synthesis of vancomycin.[9] An aryl iodide was efficiently converted into a phenol. Deprotonation of all unprotected protic groups with MeMgCl was followed by the I–Mg-exchange with *i*-PrMgCl at –40 °C. The resulting organomagnesium species was treated with $B(OMe)_3$ giving the aryl boronate, which was in situ oxidized to give the desired phenol in good yield and without noteworthy side reactions.



Scheme 1: Late stage functionalization of a complex aryl iodide by a deprotonation I–Mg-exchange sequence in Nicolaou's vancomycin total synthesis.

Also in industrial scale organomagnesium reagents are regularly employed and are of prime importance for the pharma-, fragrance- and agrochemistry. Well-known pharmaceuticals are synthesized via C–C-bond forming keysteps with Grignard reactions such as Ibuprofen, Naproxen™, Tramadol™ and Tamoxifen™.[10]

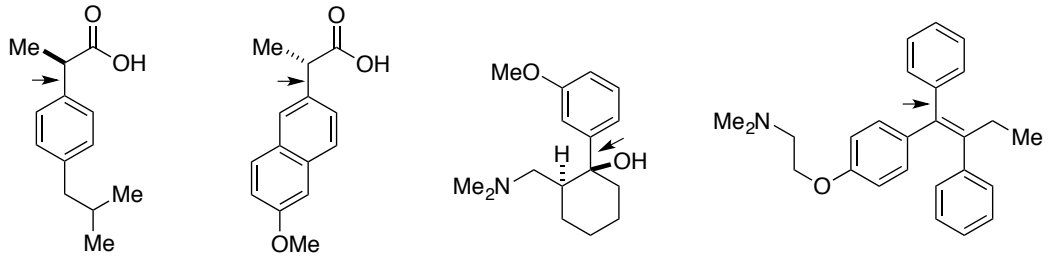
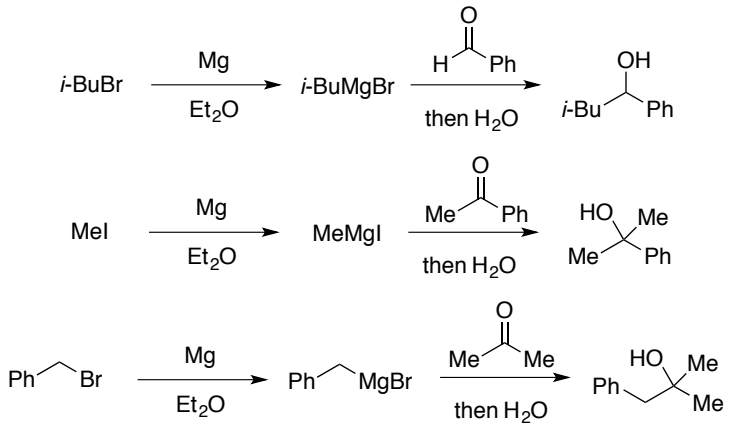


Figure 2: Important pharmaceuticals prepared with Grignard chemistry. The C–C-bonds established by organomagnesium reagents are marked with small arrows.

1.1.2 Preparation and Reactions of Grignard Reagents

Magnesium insertion into C–X-bonds

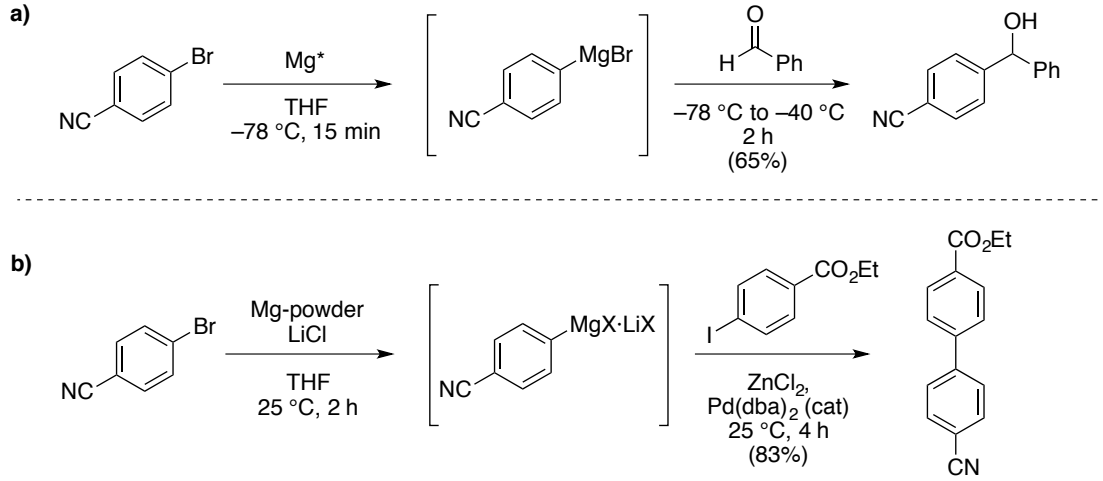
Probably most of the organomagnesium compounds are prepared by the direct reaction of magnesium metal with organic halides in aprotic ethers, the method developed in 1900 by Viktor Grignard.[11]



Scheme 2: The first published reactions of organomagnesium compounds by Victor Grignard.

The main advantage of the direct metalation is the low price of elemental magnesium and therefore it is employed, whenever the substrates and the stability of the Grignard reagents allow its preparation by this method in a laboratory as well as in a industry setting. However, the thermodynamic and heterogeneous nature of the reaction can complicate scale-up and reaction control. After an induction period, a strongly exothermic reaction is observed,

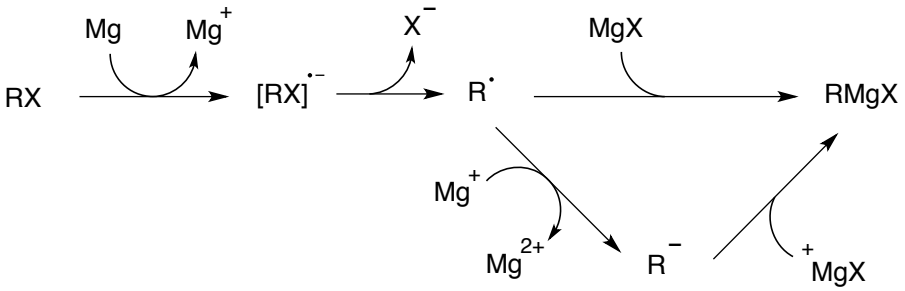
which often requires cooling. Responsible for the induction period is a passivating oxide layer at the surface of the magnesium, which may be broken up by adding an entrainment reagent (1,2-dibromoethane or iodine), by mechanical abrasion (dry stirring or sonification) or by heating under inert gas. With activated magnesium powders, i.e. Rieke-Mg (Mg*), which is prepared by the reaction of anhydrous MgX_2 with alkali metals, the metalation can be conducted at low temperatures, such as –78 °C allowing the preparation of functionalized Grignard reagents.[12] However, due to its high reactivity and its pyrophoric nature, Rieke-Mg is not easily prepared and handled and its functional group tolerance is limited.[13] Therefore, the activation of Mg by the addition of LiCl developed by Knochel serves as mild alternative.[14] This magnesiation method allows the preparation of polyfunctional organomagnesium compounds and subsequent reactions, even at room temperature.



Scheme 3: a) Magnesiation with Rieke-Magnesium tolerates a nitrile-group at –78 °C. b) Knochel's magnesiation of the same substrate with Mg-powder and LiCl at RT.

The Grignard reaction has been stated to be the "most-often-used non-trivial reaction" of organic chemistry.[15] This statement also refers to the fact that the precise mechanism of the formation Grignard reagents by the insertion of Mg into organic halides is still not fully elucidated, perhaps because it is a heterogeneous reaction occurring at a solid-liquid interface. However, experiments confirmed that the formation of Grignard reagents takes place by means of a single electron transfer. Different models have been proposed for the precise reaction pathways. Garst suggested that the formed radicals from alkyl halides can diffuse into the solution (D-Model), while Walborsky proposed "surface-adherent"-radicals (A-

Model).[16] Further it is discussed, if the intermediate organic radicals (R•) directly combine with the magnesium subhalide MgX to give the Grignard reagents (RMgX) or if the radicals are initially reduced to form the corresponding intermediary carbanions (R^-).[17]



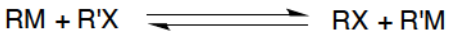
Scheme 4: Possible mechanistic pathways for the insertion of Mg into the R–X bond suggested by Bickelhaupt.[17]

It has to be considered that the discussed possible reaction mechanisms are strongly dependent on specific conditions such as the nature of the employed organic halides or solvent and therefore likely cannot be generalized for the formation of all Grignard reagents. Furthermore, is is possible that different reaction pathways might be relevant for one reaction, which explains the complexity and controversy of this research area.

The generally higher temperatures required to achieve full metalations by the classic method as well as the challenge to induce the exothermic reaction under well defined conditions limit the substrate scope, since unproductive side reactions are observed under these conditions. Some of the desired Grignard reagents are not stable at the elevated temperatures and elimination reactions or deprotonations can occur, leading to their immediate decomposition during the preparation. Another limiting reason is that many functional groups (esters, nitriles, imines, nitro-groups and hetero cycles) do react with Grignard reagents at higher temperatures, however would be tolerated at milder temperatures. Due to these preparation limitations, the advantage of the lower reactivity of magnesiumorganyls compared to lithiumorganyls could not be exploited to full extend for a long time. The emergence of mild halogen-metal exchange methods in recent years improved the accessibility to organomagnesium compounds as well as their functional group tolerance and broadened the scope of applications dramatically.

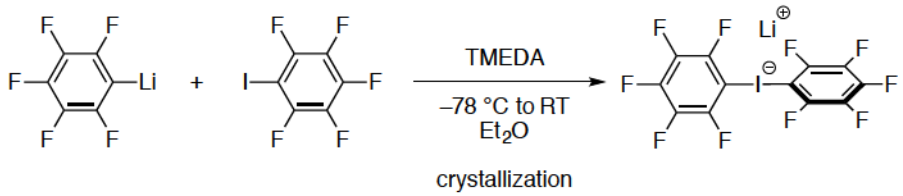
Halogen-metal-exchange

The halogen-metal exchange is a double replacement reaction (metathesis) between organic halides with halogen-metal exchange reagents. These reagents are usually commercially available and low-priced alkyl-organometallics that can easily be obtained by the direct preparation method with elemental metals. The reversible nature of halogen-metal exchange reactions generally results in the formation of the more stable carbanion intermediate ($sp > sp^2 > sp^3_{prim} > sp^3_{sec}$). Therefore, this strategy is predestined for the preparation of the arylic and vinylic organometallic reagents, which otherwise can be difficult to prepare by direct insertion reactions.



Scheme 5: Halogen-metal exchange reaction.

Depending on the substrates and conditions three different types of mechanisms have been proposed in the context of X–Li-exchange reactions. A four-center transition state model, a radical mediated mechanism by single electron transfer and a nucleophilic mechanism via "ate"-complexes.[18] In this respect, Farnham and Calabrese were able to prepare, isolate and fully characterize an iodine-ate complex (Scheme 6).[19]



Scheme 6: Iodin-ate complex prepared by Farnham and Calabrese.

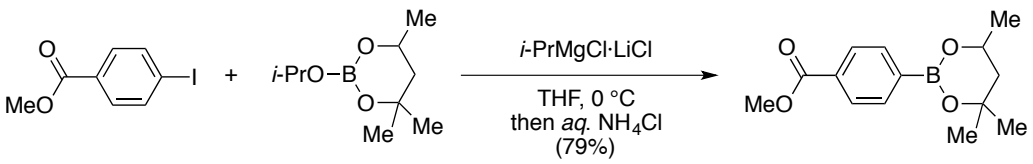
The halogen-magnesium exchange is proposed to proceed mainly by the nucleophilic mechanism via halogen-"ate"-complexes.[20] The nucleophilic mechanism can either proceed in two-steps via halogen-"ate"-intermediates or in one-step with "ate"-transition states.[21]

The advantages of halogen metal exchange reactions compared to the metalation with elemental Mg are manifold. The main advantages of halogen-metal exchange reactions are the usually lower reaction temperatures, the homogeneous reaction

conditions, the surface independence and the absence of induction time or preactivation procedures. Traditionally, the halogen-metal exchange was the method of choice to prepare lithiumorganyls, profiting from very high X–Li-exchange rates.[22] The corresponding halogen-magnesium exchange was initially discovered by Prévost,[23] but was more sporadically used to access Grignard reagents, which are difficult to prepare by the classic insertion of elemental magnesium.[24] The drawback of these reactions is the rather slow X–Mg-exchange, which hampered their wider application and only for example allowed to metalate functionalized aryl iodides at mild temperatures, but not the corresponding aryl bromides.[25] The discovery that the addition of a catalytic amount of Li(acac) can accelerate the exchange rates of I–Zn-exchange reactions by Knochel paved the way for a major breakthrough in the field.[26] The group of Knochel further investigated the effect of different Li-salts on Br-Mg-exchange reactions and developed the first and still most employed modern Br–Mg-exchange reagent *i*-PrMgCl•LiCl, which is nowadays commercially available and known as Turbo-Grignard reagent.[27]

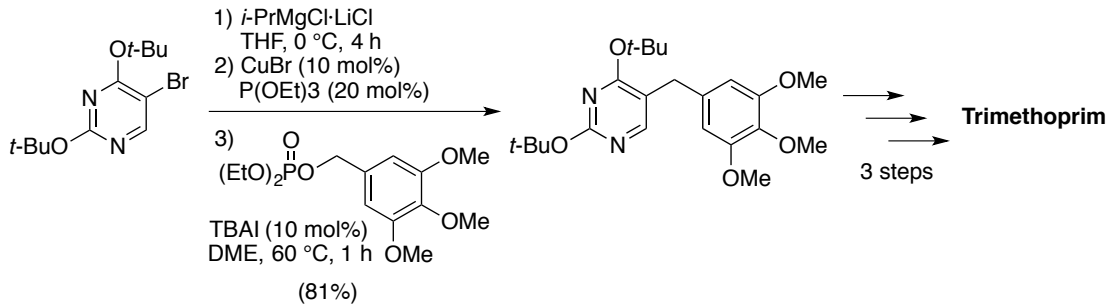
The Turbo-Grignard Reagent and Trialkylmagnesiates

Henceforward, the X–Mg-exchange reactions evolved to a powerful method to prepare various magnesiumorganyls.[28] The increased exchange rates under mild conditions, compared to the conditions necessary for the classic direct metalation with magnesium for analog substrates, allowed to exploit the lower reactivity, i.e. the higher functional group tolerance of Grignard reagents compared to Li-organyls. Chavant for example developed a convenient one pot-procedure to synthesize boronic esters.[29] Different functional groups were tolerated at 0 °C under these Barbier-like conditions.



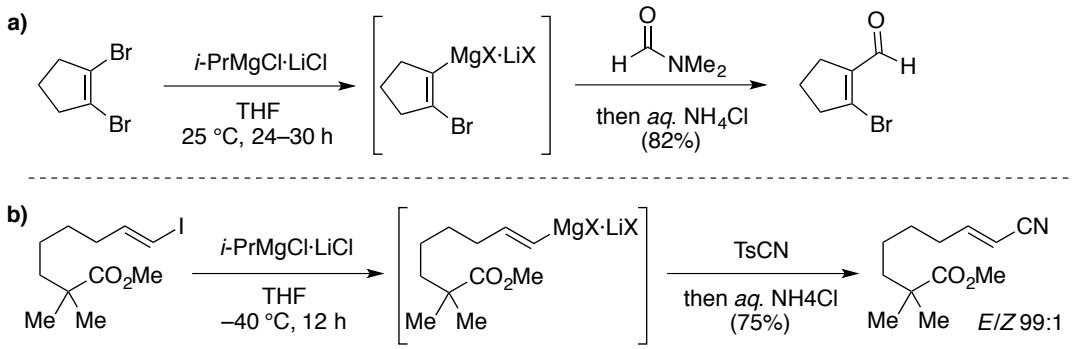
Scheme 7: Chauvant's in-situ synthesis of functionalized boronic esters tolerating a methylester-group.

Moreover, various organomagnesium compounds are now accessible from brominated highly substituted aromatic heterocycles with high efficiency.[30] This allows the synthesis of different pharmaceutical ingredients,[31] like the antibiotic trimethoprim.[32]



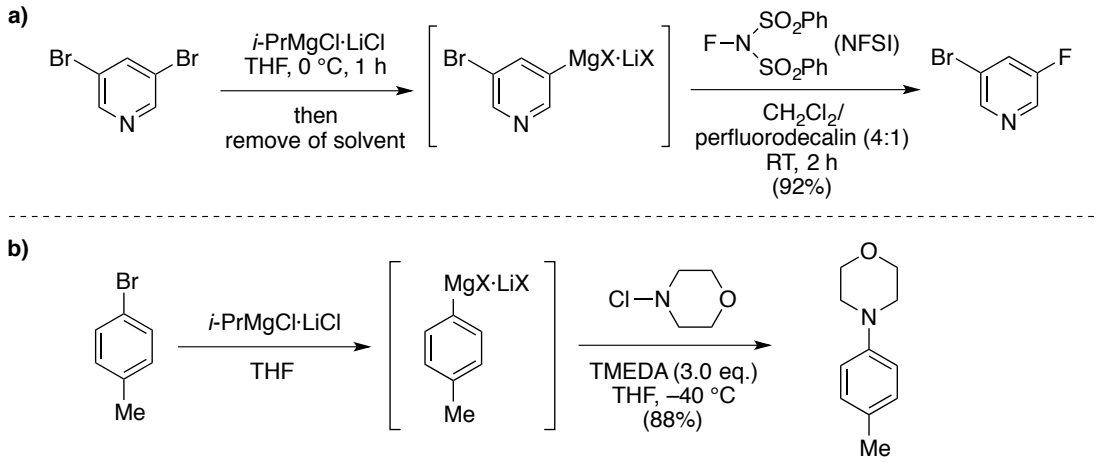
Scheme 8: The LiCl accelerated Br–Mg-exchange of a bromo-uracil-derivative allows to synthesize the antibiotic trimethoprim in 4 steps.

Also cyclic 1,2-dibromo-alkenyls prone for β-elimination[33] and alkenyliodides without chelating groups[34] were successfully functionalized after the effective halogen-metal exchange with the Turbo-Grignard reagent under mild conditions.



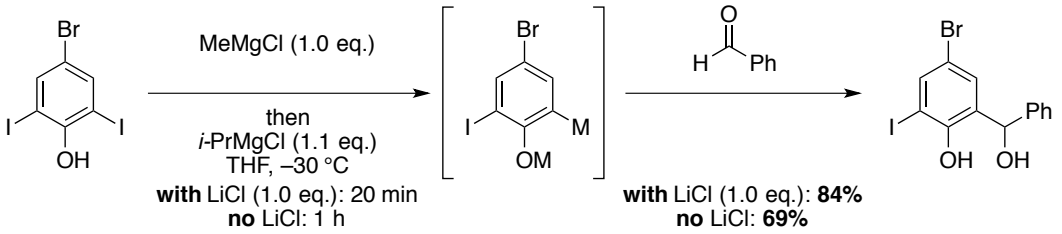
Scheme 9: a) High yielding *mono*-functionalization of 1,2-dibromocyclopentene at 25 °C. b) Stereoselective functionalization of an alkenyl iodide at –40 °C tolerating i.e. a methyl ester group.

Under specific conditions, the obtained Grignard reagents can even be fluorinated[35] or after addition of TMEDA reacted with chloramines to give not the expected chlorinated products, but the corresponding amines without the need of transition metals.[36]



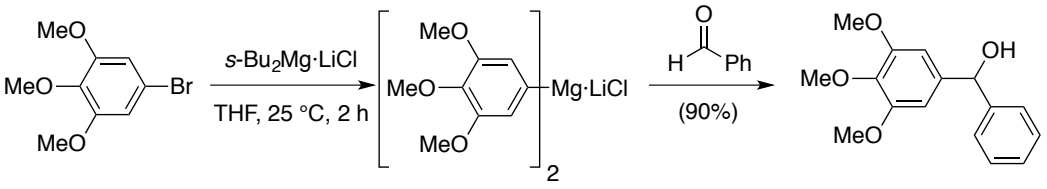
Scheme 10: a) Direct fluorination by reacting the intermediate organomagnesium reagents with NFSI in the presence of fluorinated solvent. b) Direct amination of Grignard reagents by the reaction with bisalkylated chloramines in the presence of TMEDA at –40 °C.

Furthermore, the deprotonation-metalation sequence to functionalize polyfunctional aromatics bearing an unprotected hydroxyl group could be improved in the presence of LiCl.[37] Besides the higher reactivity, a better solubility of the intermediary phenolate reagents was recognized.



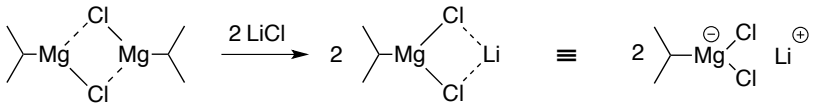
Scheme 11: Acceleration of the I–Mg-exchange in the presence of LiCl in a deprotonation-metalation sequence and improved reaction outcome in the reaction of the intermediary magnesiated magnesium phenolates with electrophiles.

Very electron-rich aromatic bromides are best metalated with secondary *bis*-alkylmagnesium reagents such as *s*-Bu_2Mg•LiCl, which can be easily prepared by mixing *s*-BuMgCl with *s*-BuLi in a one to one ratio.[21] These reagents show an even higher capacity to accelerate the exchange reactions compared to the corresponding bis-alkylmagnesium reagents without LiCl as well as the Turbo-Grignard reagent.



Scheme 12: The secondary bis-alkylmagnesium reagent *s*-Bu_2Mg•LiCl allows the highly efficient conversion of an very electron rich bromo-trimethoxybenzene to the corresponding Grignard reagent.

A better solubility of the Turbo-Grignard reagents accompanied with an increased kinetic basicity favoring X–M-exchange over the nucleophilic attack on functional groups has been observed in these examples. These findings have been suggested to be a result of the capability of LiCl to deaggregate dimers of *i*-PrMgCl forming a bimetallic *i*-PrMgCl•LiCl complex displaying an increased magnesiate character.[27, 34]



Scheme 13: Proposed role of LiCl explaining the increased reactivity of the Turbo-Grignard reagent by deaggregation and formation magnesiate species.

Quantum chemical calculations by Knochel propose that the increased electronic density at the magnesium center of such a LiCl-complex decrease the reaction energy barrier of halogen–metal exchange reactions.[21] The proposed complex could not be structurally elucidated by X-ray crystallography yet, since solely adducts that are isostructural to crystals obtained from pure RMgX solutions could be found.[38] Noteworthy, the group of Mulvey was able to confirm a dinuclear structure of the magnesium amide base TMPMgCl and most intriguingly found the crystallographic proof of a four membered MgClLiCl-ring in the related Knochel-Hauser-base complex TMPMg•LiCl.[39] For both compounds, almost similar ^{1}H-NMR and ^{13}C-NMR shifts were observed in deuterated THF, however the coordination of Li in the LiCl-complex in solution could be confirmed by ^{7}Li-NMR.

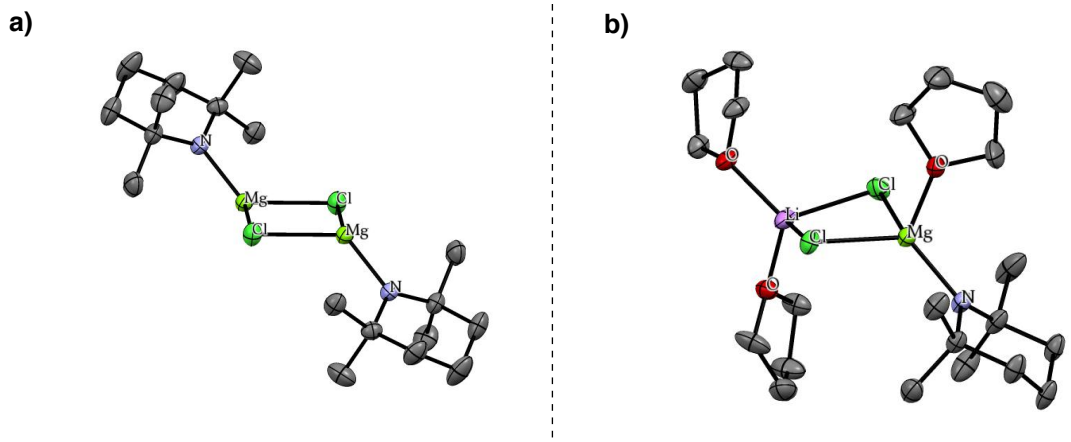
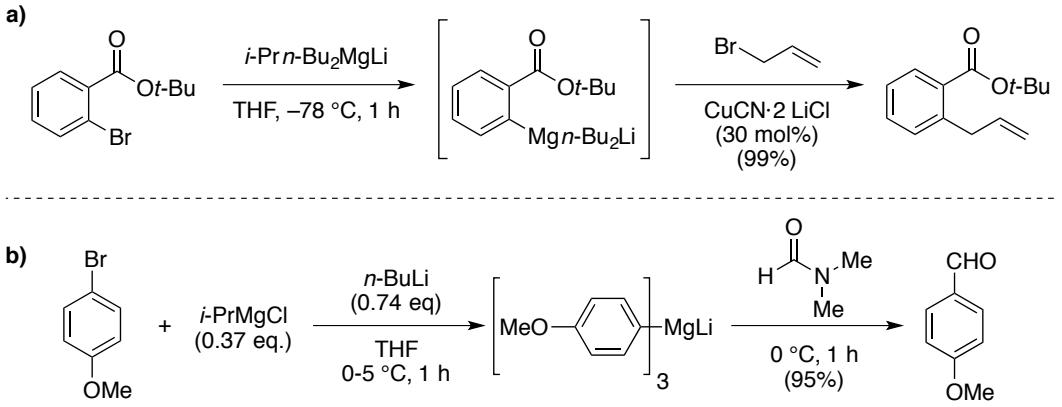


Figure 3: a) The dimeric crystal structure for TMPMg: [TMP(THF)Mg(μ-Cl)$_2$Mg(THF)TMP] with coordinating THF and hydrogen atoms omitted for clarity (CCDC 690058). b) The magnesiate crystal structure found for TMPMg•LiCl: [(THF)$_2$Li(μ-Cl)$_2$Mg(THF)TMP] with hydrogen atoms omitted for clarity (CCDC 690059).

Electrical conductivity measurements indicate that in solutions of *i*-PrMgCl as well as of *i*-PrMgCl•LiCl ate complexes are present and that the degree of magnesiate formation and heterolytic dissociation is strongly enhanced upon the addition of LiCl.[40] These observations make the proposed magnesiate character plausible.

A further support is the fact that also other bimetallic ate complexes of the form "$R_3Mg^-Li^+$" are known to have an increased reactivity compared to their neutral Grignard counterparts.[41] The triorganomagnesiates were first explored by Wittig[42] and in 2000 introduced by Oshima as powerful halogen-metal exchange reagents to prepare higher order aryl- and alkenylmagnesium reagents from the corresponding halides.[43] Probably the most often employed trialkylmagnesiate exchange reagent *i*-Pr*n*-Bu$_2$MgLi can be conveniently prepared by mixing *i*-PrMgCl with two equivalents *n*-BuLi and is in the meantime even commercially available. The resulting magnesiates are less reactive than the corresponding lithium-organyls, though can be assumed to be more reactive than RMgX•LiCl compounds. Therefore, they display an interesting reactivity profile that allows fast metalations at low-temperatures while tolerating functional groups.[44] Gallou and coworkers published an interesting study that showed the improved stability and reactivity profile of trialkylmagnesiates compared to Li-organyls in the functionalization of 4-bromoanisol.[45] In the same paper the Novartis research group reported an in-situ preparation protocol, i.e. the addition of *n*-BuLi to a

mixture of *i*-PrMgCl and the aryl halogenide, which allowed the direct functionalization at non-cryogenic temperatures.

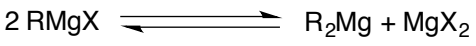


Scheme 14: a) The halogen-metal exchange at low temperature with R_3MgLi is highly efficient and tolerates functional groups that would react with *n*-BuLi. b) An in-situ procedure developed by a Novartis Research Group allows the efficient use of magnesiates at non-cryogenic temperatures.

Alternative preparations of Grignard reagents are directed deprotonations of (hetero-)arenes with the before mentioned magnesium amide bases (i.e. TMPMg•LiCl) and transition-metal catalyzed hydromagnesiations of alkenes or alkynes.

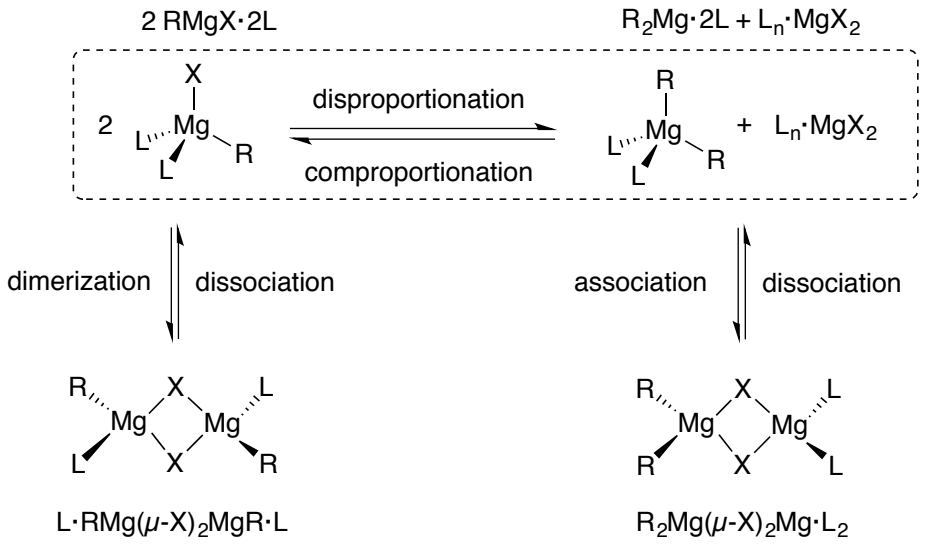
1.1.3 Constitution and Structure Elucidation of Grignard Reagents

In 1929, Wilhelm Schlenk[46] published a seminal paper about the constitution of Grignard reagents in solution.[47] Repeated crystallization at low temperature allowed to obtain pure Grignard reagents in Et_2O, free of inorganic salts and with an overall molecular ratio of Mg to halide (X) of 1:1. Addition of dioxane to these solutions led to the formation of precipitates, which had a molecular ratio of Mg:X < 1. From these observations it can be concluded that inorganic MgX_2 is formed from pure Grignard reagent and that the residual solution contained diorganyl magnesium compounds of the form R_2Mg. From these and further experiments the following equilibrium, known as the Schlenk-equilibrium, was postulated by Schlenk.



Scheme 15: The classic Schlenk equilibrium.

Prompted by the rise of advanced analytical methods in the middle of the 20th century, the understanding of the structure of Grignard reagents has increased significantly.[48] Tracer studies with labeled $^{28}MgBr_2$ confirmed the dynamic nature of the Schlenk equilibrium by the observation of a statistical exchange of the radioisotopes between the Grignard reagents and the inorganic salt.[49] Molecular weight measurements (ebullioscopy and vapor pressure osmometry)[50] allowed to expand the classic Schlenk-equation with self association equilibria of the individual Schlenk components e.g. with a dimerization equilibrium. The measurements revealed that very diluted solutions (≤ 0.05 M) of organomagnesium bromides and iodides in Et_2O and THF indeed are monomeric. While at higher concentrations in Et_2O a tendency to form dimers and oligomers was observed, this trend is less pronounced in THF, where also monomers are found at high concentrations. Furthermore, calorimetric measurements gave insights into the constitution of Grignard reagents in solution.[51] Shifts in infrared spectra (IR) were interpreted as support for the existence of dimers and further suggest the coordination of solvent molecules, however these correlations entail a high degree of uncertainty, hence the value of IR-spectroscopy for structure elucidation is rather limited.[52] Due to the very fast exchange rates for most Grignard reagents, NMR-spectroscopy does not allow to differentiate between RMgX and R_2Mg at room temperature and only average signals can be observed. However, measurements at cryogenic temperatures or the addition of coordination agents allow to make statements about the individual composition of diverse Grignard reagents. ^{1}H-NMR spectroscopy experiments are complemented by ^{13}C-NMR, ^{19}F-NMR and recently by DOSY-NMR experiments.[53] Moreover, metal-NMR measurements (^{25}Mg) are feasible for the characterization of organomagnesium compounds.[54] Conductivity measurements indicate the amount of ionic species in pure Grignard reagent is so low that ionization can be more or less neglected for their description.



Scheme 16: A more current, but still simplified view of the equilibria of the species that can be present in solutions of organomagnesium reagents in donor solvents (L) showcased as the predominately tetrahedrally coordinated magnesium.

Special X-ray scattering techniques like EXAFS (extended X-ray absorption fine structure) enable to gain information about inter- and intra-atomic distances directly in solution.[55] Classic X-ray diffraction techniques of crystalline Grignard reagents allow valuable insights into the spatial structure and coordination spheres in the solid state.[56] These findings support the structure elucidation of Grignard reagents, since it is assumed that the structures found in the solid state can be more or less also encountered in solution.

The preferred coordination number of magnesium of inorganic Mg^{2+}-salts is six, as found in the aqua-complex of $[Mg(H_2O)_6]^{2+}$. To attain this ideal coordination state, the ligands are required to be small and the charge on the metal has to be high (i.e. +2). These conditions are rarely found in organomagnesium compounds, since the organic groups, as well as the coordinating ligands are sterically demanding and the charge is less than +2. Therefore, the magnesium in by far the most Grignard reagents is usually tetrahedrally coordinated and this motif is found in monomeric [RMgX•2L], dimeric [L•RMg(μ-X)$_2$MgR•L] (Scheme 16) and under solvent free conditions in oligo- or polymeric structures [(μ-R_2)Mg(μ-R)$_2$Mg]$_n$. However, there are cases where the magnesium was found to have a lower coordination number e.g. 2 in [supermesityl$_2$Mg] or 3 in magnesiates and NHC-ligated magnesium complexes. Also higher coordination numbers like 5 in

[MeMgBr•3 THF] are found and even hexa-coordinated complexes have been characterized in case of intramolecular coordinating poly-ethers or for Mg-acetylides [$(RC{\equiv}C)_2Mg$•4 THF] (Figure 4).

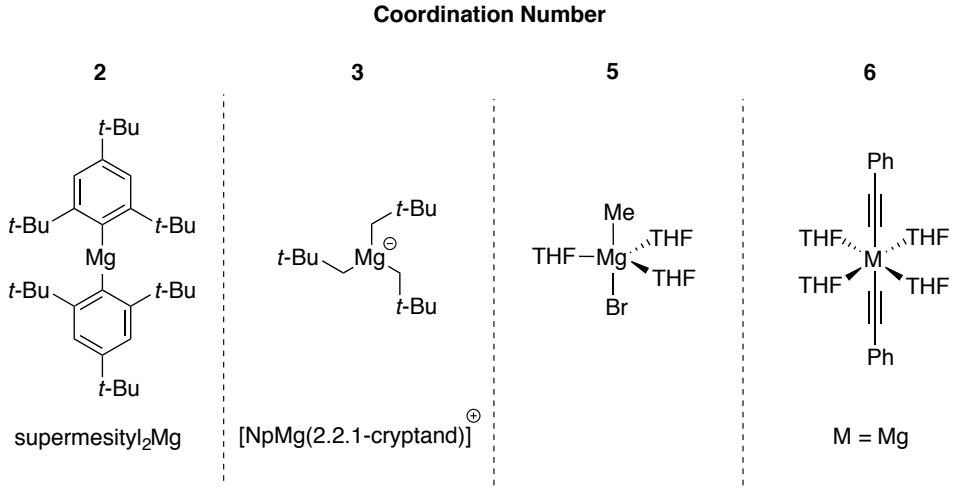
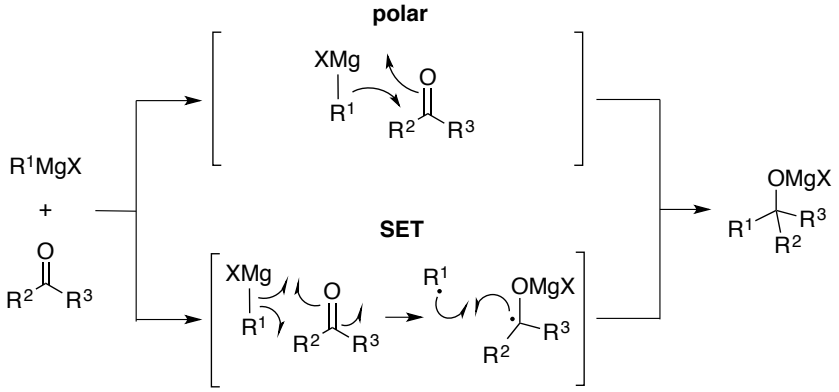


Figure 4: Other coordination numbers than 4 in organomagnesium compounds. Lower coordination numbers are found in Grignard reagents with exceptional high steric hindrance or in magnesiates. Higher coordination numbers in case of sterically less demanding organic residues.

Organomagnesium reagents usually contain diverse species, which are interlinked with each other by dynamic ligand exchange equilibria around the magnesium center. The shift of these equilibria depend decisively on factors like temperature, concentration, coordinating properties of the solvent and the halide-ions as well as on the electronic and steric properties of the organic residues. More and more of the experimental insights are supplemented by theoretical calculations.[57]

1.1.4 Mechanisms of the addition of Grignard reagents to Carbonyls

Similar as for the structure and composition of Grignard reagents, the detailed mechanism of one of the most crucial C–C-bond forming reactions, the 1,2-addition of organomagnesium reagents to carbonyls have been investigated in detail and was discussed for decades. This indicates that the mechanism is intricate and depends on several factors such as the organic residue, halogen, solvent, temperature and concentration. Two potential mechanistic pathways are considered to take place: a single electron transfer mechanism (SET) or a polar mechanism (Scheme 17).[58]

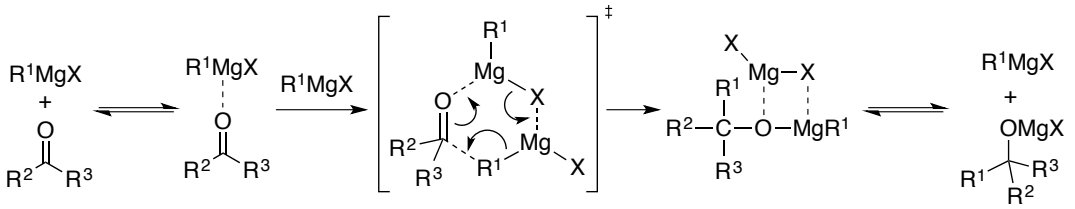


Scheme 17: The addition of Grignard reagents to carbonyls is considered to take place via a polar and a single electron transfer (SET) mechanism.

In general, the polar mechanism is regarded as the dominant reaction pathway for most reactions. The SET-mechanism was found to be dominant with highly steric hindered Grignard reagents and benzylic ketones. All addition reactions are basically irreversible.

Polar mechanism

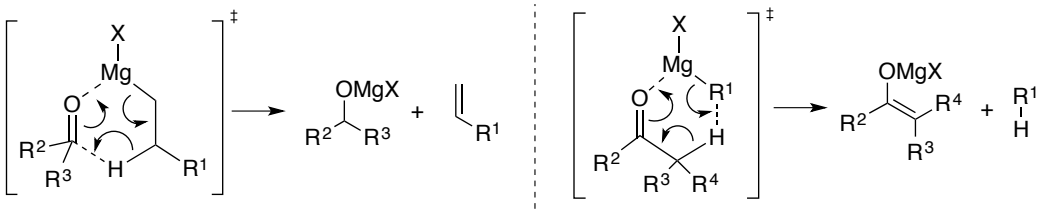
In seminal investigations Swain and Boyle found that pre-addition of $MgBr_2$ to *i*-Pr_2C=O improved the yield of the reaction with *n*-PrMgBr from 36% to 65% at the expense of the unproductive reduction pathway.[59] From this result and previous investigations they concluded that the carbonyl oxygen atom is coordinated by a Mg^{2+}-cation and proposed that without an additive, a Grignard molecule R – MgX coordinates to the oxygen. By this, the polarization of the carbonyl-functionality is increased and allows a second Grignard molecule to attack the more electrophilic C-atom. Later, Smith and Su also found spectroscopic evidence for the formation of a complex[60] and Ashby proposed, based on kinetic measurements and previous findings, a widely accepted termolecular mechanism via a cyclic 6-membered transition state (Scheme 18).[61]



Scheme 18: Ashby's widely recognized proposal: Grignard reagents react with carbonyls in a termolecular mechanism via 6-membered cyclic transition state.

Related 6-membered TS geometries can also explain the fact that Grignard reagents bearing a H-atom in β-position tend to reduce carbonyls while forming

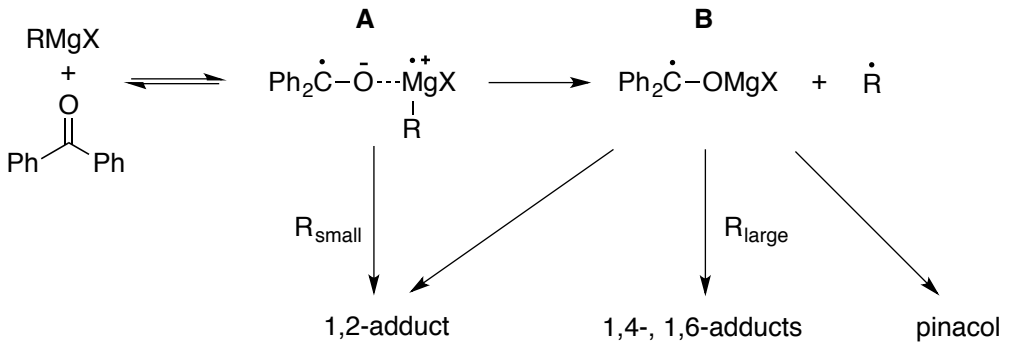
the corresponding alkene by a β-hydride elimination (Scheme 19).[58] Furthermore, the formation of magnesium-enolates from Grignard reagents and carbonyls that bear a hydrogen in α-position can satisfyingly be interpreted. In the context of the 1,2-addition of Grignard reagents, these two reactions are the most often encountered side reactions and limit the substrate scope of Grignard additions.



Scheme 19: Reduction of a carbonyl with a Grignard reagent (left) and the formation of a magnesium enolate from a carbonyl bearing a H-atom in α-position (right).

SET Mechanism

Holm and Crossland investigated the reaction of *t*-BuMgCl with various benzophenones.[62] The product distribution was found to be strongly dependent on steric effects and different ratios of 1,2-, 1,4- and 1,6-addition products, as well as benzopinacols were observed. However, the overall rate of the reaction was not influenced by steric factors, which indicated an initial rate limiting step. Based on these findings this step was suggested to be the formation of a *t*-Bu radical and the benzophenone ketyl radical anion by a one electron transfer. By considering also the reaction of MeMgCl with benzophenones and further kinetic studies, Yamataka and his group proposed the existence of equilibrium prior to the rate determining step (Scheme 20).[63]



Scheme 20: Yamataka's detailed description of the radical mechanism for the reaction of benzophenones with Grignard reagents.

While the small MeMgCl is suggested to entirely react via intermediate **A**, the second reaction pathway via intermediate **B** becomes predominant for nucleophiles with steric bulky groups such as *t*-BuMgCl. This explains the observed kinetics as well as the product distribution and hence the isomerization of intermediate **A** to intermediate **B** is considered to be the rate-determining step in this case.

Computational Studies

In silico studies give more and more insights into the reaction mechanism of Grignard reagents with carbonyls, mainly for short chained reagents such as MeMgX. These theoretical predictions allow to take solvent coordination, the role of the halide as well as the Schlenk- and dimerization equilibria into account and hence enable a more detailed view on the transition state geometries. Studies by Yamabe[64, 58] and later by Kato[57] suggest that the classic 6-membered transition state geometry should be revised to a dimeric 4-membered reaction path (Figure 5). Yamabe calculated a dichlorine bridged transition with higher coordinated magnesium-atoms for the reaction of MeMgCl with formaldehyde in Me_2O, while Kato's model with the steric more demanding Et_2O in the addition to acetone results in a similar, but monochloride bridged transition state with a lower coordination mode. The solvation structure of the TS calculated by Kato is similar to the structure of the Grignard reagent-acetone complex i.e. the reactants, which is in accordance with an early TS and consistent with the observed exothermicity of the reaction (Hammond's postulate).

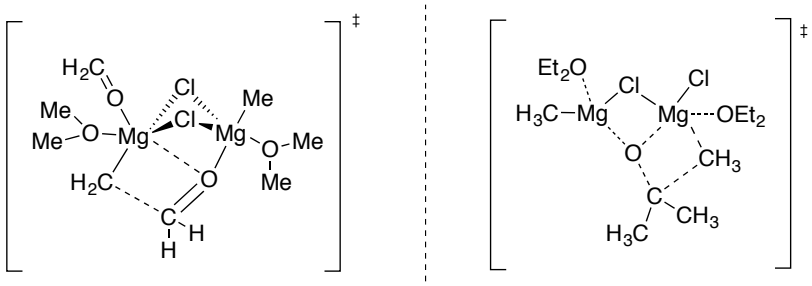
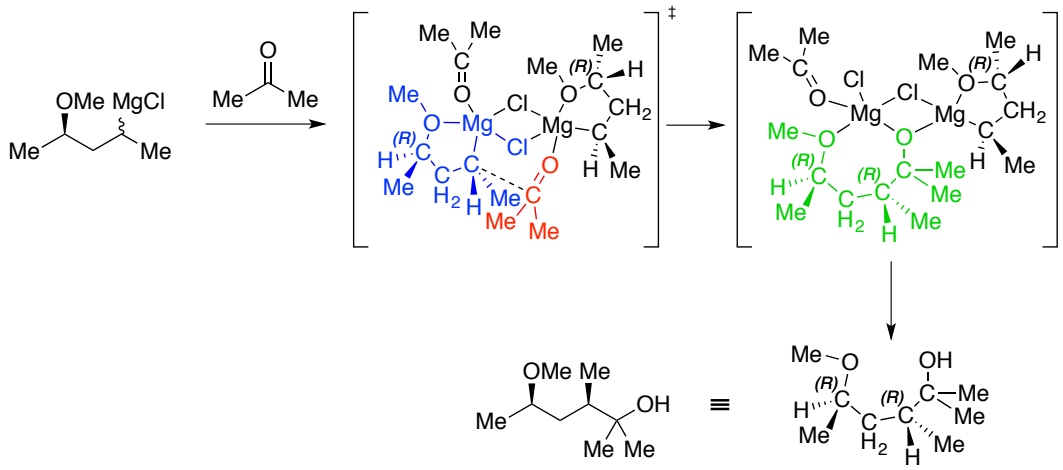


Figure 5: Yamabe calculated a dichlorine-bridged 4-membered TS for the addition of MeMgCl to formaldehyde in Me_2O (left) and Kato a monochlorine-bridged TS for the addition of MeMgCl to acetone in Et_2O (right).

Yamabe also computed a chelation controlled addition model confirming the experimental findings by Miles[65] about the stereochemical outcome of the reaction of chiral χ-alkoxy magnesium halides with ketones (Scheme 21).



Scheme 21: Chelation model for the stereoselective addition of chiral χ-alkoxy Grignard reagents to acetone.

Furthermore, his group modeled similar dichlorine-bridged TS-geometries for the reaction of *t*-BuMgCl with with $Ph_2C{=}O$, a reaction following predominantly the SET pathway (Figure 6).[58]

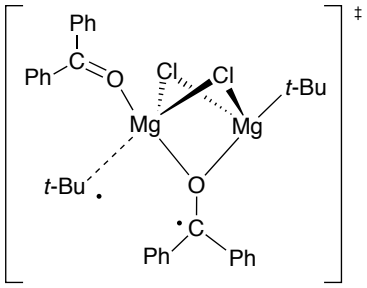


Figure 6: Yamabe's calculated TS-structure for the SET reaction pathway.

1.1.5 Bifunctional Organomagnesium reagents

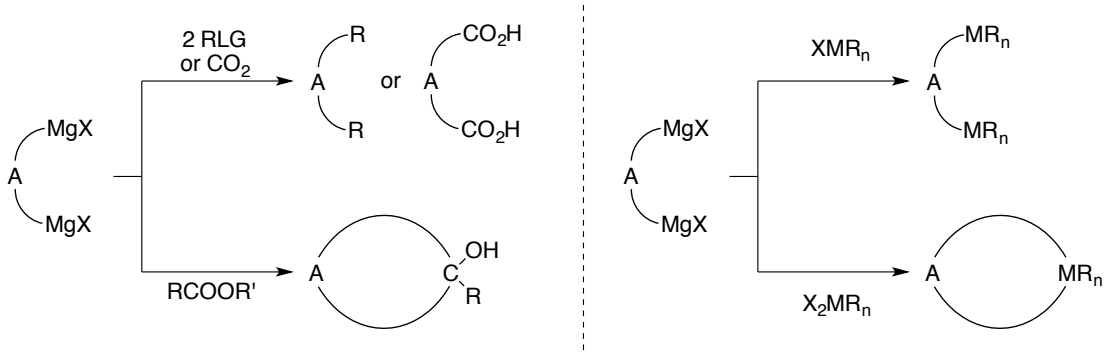
Preparation

While the preparation of short-chained di-Grignards is synthetically challenging due to side reactions, the synthesis of longer-chained reagents can generally be achieved by metalation of the dihalides with elemental magnesium or with halogen-metal exchange reagents.[66] In case of some arenes and alkenes and dienes, the magnesium has to be activated, respectively more reactive X–M-reagents (Turbo-Grignard, magnesiates) are necessary. Traditionally, the synthesis from the corresponding mercury compounds, which in turn are

prepared by treating dihalides with sodium amalgam, was a common strategy.[67] Since the mercury compounds can effectively be purified, this synthetic pathway allows the synthesis of salt-free and pure cyclic organomagnesium compounds.

Reactivity

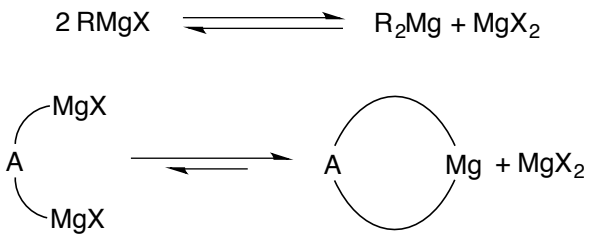
Di-Grignard reagents (XMg–R–MgX) are intriguing compounds from a synthetic point of view. Same as their monofunctional counterparts (R–MgX), they serve as nucleophiles, however are able to react twice and depending on the electrophile, either give bifunctional or cyclic products. Besides reactions to form C–C-bonds other C–heteroatom-bond forming reactions allow to access diverse acyclic or cyclic derivatives. In particular, transmetalations have been a core application of these Grignard reagents and allowed to study the properties of various bifunctional organometallic derivatives.



Scheme 22: Application of bifunctional Grignard reagents to form C–C-bonds and to obtain bifunctional or cyclic products or to prepare other acyclic or cyclic derivatives (M = B, Al, Ga, In, Si, Ge, Sn, Sb, Zr, Pt, Rh, Ir, Ti etc.)

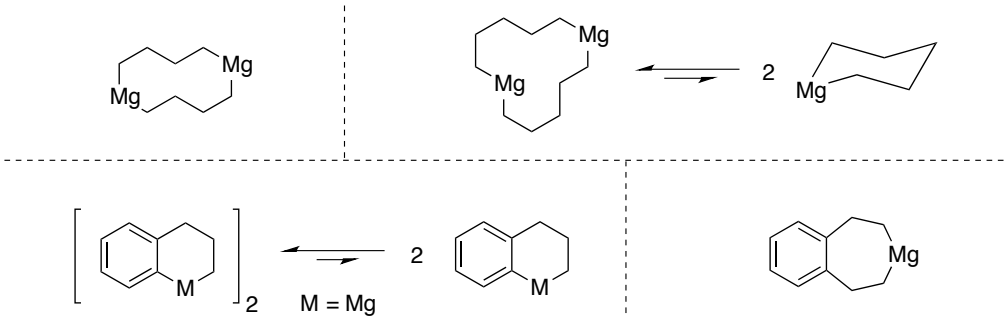
Structure

Another fascinating aspect, inherent to bifunctional organomagnesium compounds is that they often display unique structures.[68] The Schlenk-equilibrium of di-Grignard reagents is generally shifted in comparison to their monofunctional analogues, since the formation of metalla-cyclic structures is entropically favored.



Scheme 23: Classic Schlenk-equilibrium of monofunctional compared with bifunctional organomagnesium reagents.

Depending on the backbone of the organometallic reagents (i.e. the length of the alkylchain) and other variables like temperature, concentration and solvent, the cyclic structures are usually present as monomers or dimers, though also oligomers, polymers and equilibria between different structures are observed.[69] Generally, the existing structure is the result of an interplay of torsional and ring strain. Due to the preferred large C–Mg–C bond-angle of 120° to 140°, small alkyl-rings would be highly strained. Therefore, short-chained bifunctional Grignard reagents display a high tendency to form dimeric structures with 10 or 12 membered rings. For instance, 1,4-dimagnesiumbutane was found to be fully dimeric in THF, while its 1,5-analog is present as a monomer-dimer-mixture. Six carbon atoms between the two carbon-bound magnesium atoms were found to allow the formation of a strain-free monocyclic structure. For aryl-alkyl-Grignard reagents, the same trend was observed.



Scheme 24: Short chained (≤4) bifunctional Grignard reagents preferentially form dimeric rings in solution, while longer chains (≥6) are present as monomers. Illustrated without solvation.

Recently, Westerhausen prepared several di-Grignard complexes and after precipitation of magnesium halides with dioxane, was able to crystallize and characterize dimagnesiumcycloalkanes with ring sizes from 8 up to 18 atoms.[70] From highly concentrated solutions in THF polymeric "zig-zag"-strands of the form $[(THF)_2Mg\{\mu\text{-}(CH_2)_n\}]_m$ with n = 4 or 6 could be crystallized. DOSY-NMR experiments suggest the presence of the corresponding dinuclear structures in solution.

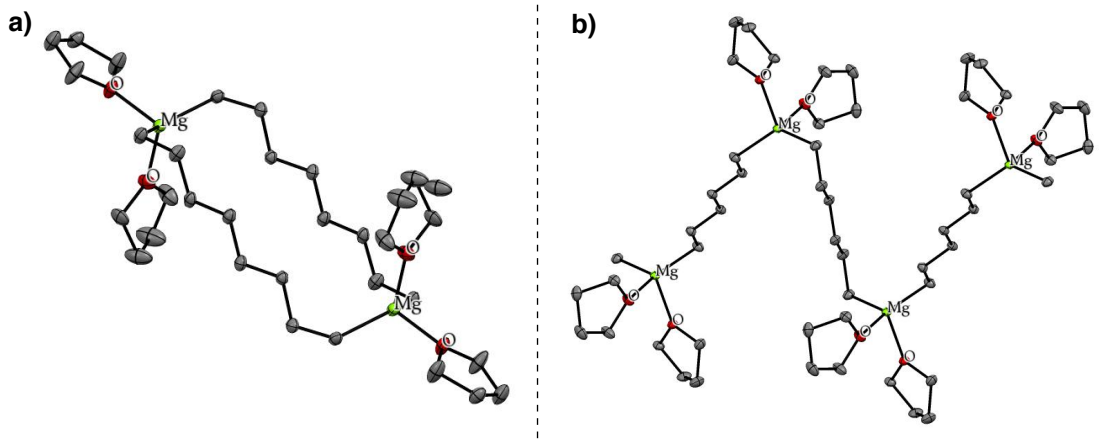


Figure 7: a) The so far largest fully characterized 18-membered-ring dimagnesiacycloalkane $[(THF)_2Mg\{\mu\text{-}(CH_2)_8\}]_2$ (CCDC 1439339). b) A section of the polymeric "zig-zag"-strand $[(THF)_2Mg\{\mu\text{-}(CH_2)_6\}]_\infty$ crystallized from a highly concentrated THF solution (CCDC 1439338).

In addition, it was found that tertiary alkanediide ligands exhibit smaller C–Mg–C bond angles, which allowed to crystallize and characterize mononuclear tetramethyl-substituted mangnesiacyclohexane $[(THF)_2Mg\{CMe_2(CH_2)_3CMe_2\}]$ with an exceptional small C–Mg–C bond angle of approx. 110°.

Intriguingly, Bickelhaupt reported that bifunctional oxygen-containing organomagnesium reagents are purely monomeric, probably due to the strong intramolecular coordination measured for these compounds.[68, 71]

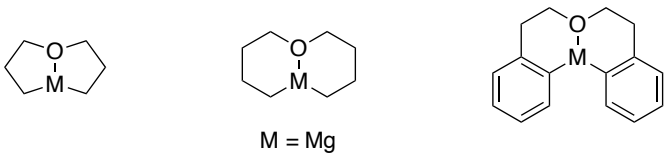
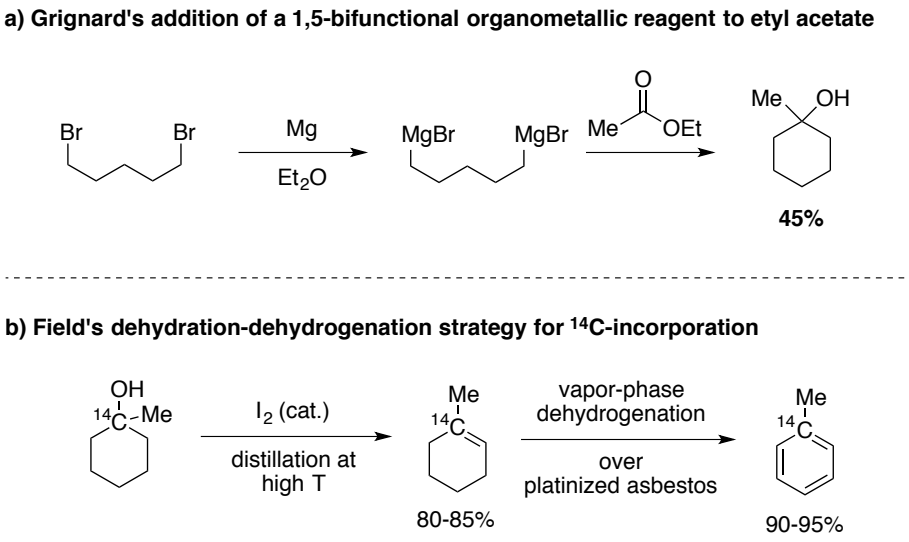


Figure 8: Mononuclear structures found for oxygen containing bifunctional Grignard reagents.

1,5-Bifunctional alkylmagnesium reagents

Victor Grignard prepared the first 1,5-bifunctional organomagnesium reagent with a fully saturated alkyl-chain by a direct magnesiation of 1,5-dibromopentane with elemental magnesium (Scheme 25).[72] The prepared bifunctional organomagnesium reagent was added to ethyl acetate and a cyclic tertiary alcohol was obtained. The reaction constitutes the first example of a double nucleophilic attack of a bifunctional organometallic reagent to an ester forming a six-membered cycle by means of [5+1]-ring-formation. Later this reaction was utilized by Fields and coworkers in a strategy to incorporate a radioactive

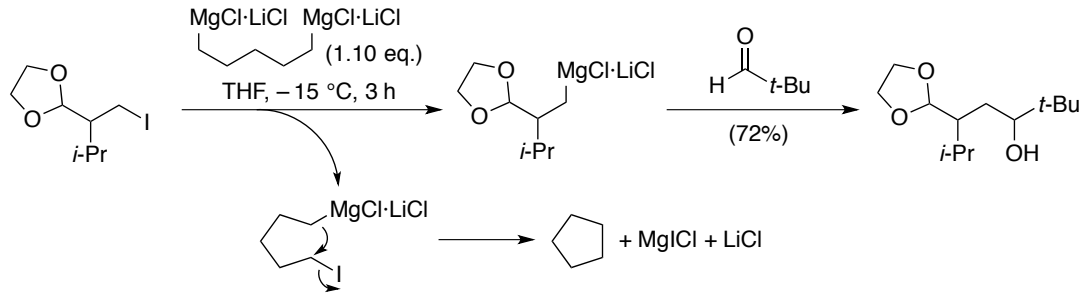
^{14}C-isotope into an aromatic ring (Scheme 25b).[73] However, to achieve arene-formation, harsh reaction conditions for the dehydration of the obtained alcohol and the following dehydrogenation of the six-membered cyclohexene had to be employed.



Scheme 25: a) Viktor Grignard's double addition of a 1,5-bifunctional organomagnesium reagent to a ethyl acetate to form a cyclic tertiary alcohol. b) dehydration-dehydrogenation strategy employed on the corresponding C^{14} tertiary alcohol under harsh conditions.

The opportunity to introduce the unsaturation already before the [5+1]-ring-formation by reacting corresponding unsaturated 1,5-bifunctional organomagnesium reagents with esters, would allow the formation of an aromatic system directly by a 1,4-elimination of the intermediary alcohol under mild conditions. By this, ubiquitous carboxylic acid esters could be coupled at mild temperatures with diverse aromatic moieties. Therewith, such a method would complement classic transition-metal catalyzed cross coupling reactions.

Another interesting application of a 1,5-bifunctional Grignard reagent associated with LiCl is the elegant use as a halogen-metal exchange reagent to metalate sp^3-hybridized iodides bearing neighboring coordinating heteroatom-groups.[74] The formation of cyclopentane is the driving force of the reaction and shifts the equilibrium into the desired direction.

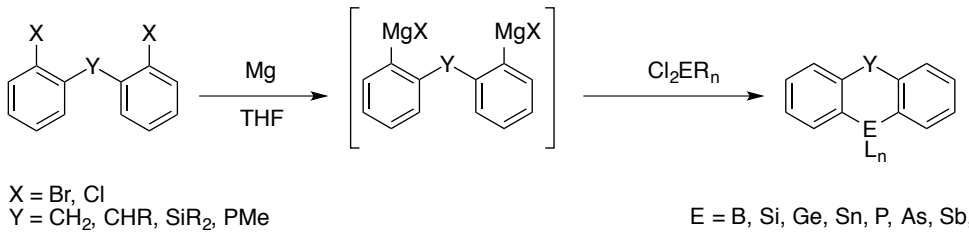


Scheme 26: After the initial exchange reaction the intermediary 5-iodo-pentylmagnesium chloride undergoes an intramolecular S_N2-substitution forming cyclopentane, which shifts the equilibrium into the desired reaction.

This strategy is probably best compared with the use of *t*-BuLi, where a subsequent deprotonation-elimination reaction removes one of the products and enables to realize X–Li-exchange reactions with unfavorable equilibria. In certain cases, the use of this novel 1,5-bifunctional X–Mg-exchange reagent might be an alternative to the employment of the much more basic and pyrophoric reagent *t*-BuLi.

1,5-bifunctional bis-arylmagnesium reagents

Various 1,5-bifunctional bis-arylmagnesium reagents have been conveniently prepared by the direct reaction of the corresponding dihaloaryl-derivatives with elemental magnesium.[75] The Grignard reagents were treated with different electrophiles to give various heteroatom containing dihydroanthracenes and other corresponding heteroatom-containing cyclic derivatives. Also the synthesis of an unsymmetrical silaanthracene with a methyl-substituent *ortho* to the silicon-atom was reported.



Scheme 27: The preparation of various 1,5-bifunctional bis-arylmagnesium reagents and their use to form diverse cyclic-heteroatom-containing anthracene-type compounds.

1.2 Stereoselective Arene-forming reactions

Benzene and its non-substituted linearly-fused polycyclic analogues have a highly symmetric flat structure. Therefore, it is somewhat counterintuitive that the de-novo formation of aromatic rings offers the opportunity to develop stereoselective reactions. After pioneering efforts starting in the 1950s, reactions applying this concept have emerged more and more over the recent two decades and are contributing to a vibrant field of research. Stereoselective arene-forming reactions offer the opportunity to prepare various stereochemically complex structures in isomerically pure form such as molecules with central, helical,[76] planar,[77] inherent[78] and axial[79] chirality (Figure 9). Another interesting substance class that might be accessible in future are chiral catenanes i.e. chiral mechanical interlocked molecules.[80] The de novo synthesis of arenes complements the "post"-functionalization methods of existing aromatics and offers the means to develop convergent synthetic pathways, which are highly desired, considering the nowadays required high molecular complexity. Within the scope of stereoselective arene-forming reactions, the atroposelective synthesis of axially chiral compounds is the most investigated field underlining the importance of these products.

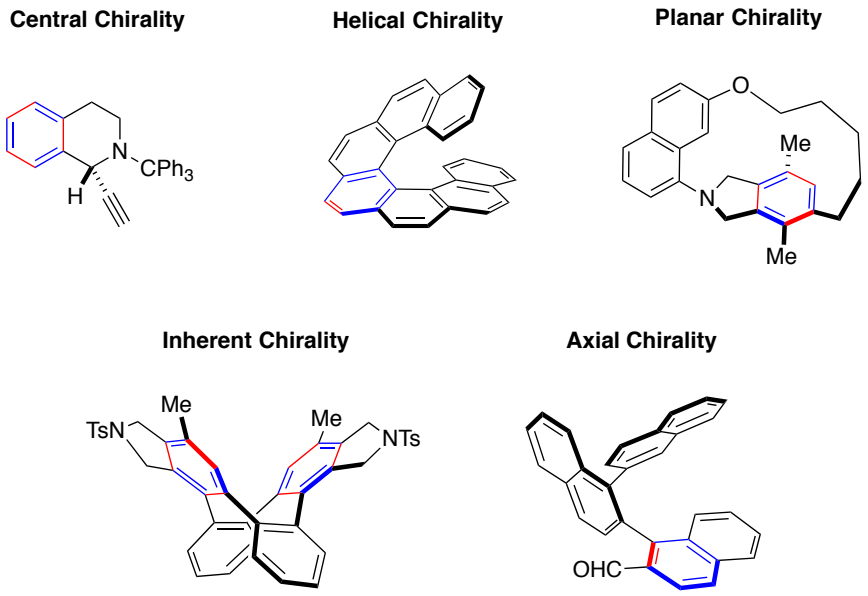


Figure 9: Outline of molecules with different chiral motifs prepared by stereoselective arene-forming reactions.

1.2.1 Axially Chiral Compounds

Axial chirality is a structural feature frequently encountered in natural products, medicinal chemistry and most often in ligands that are employed in stereoselective synthetic chemistry.[79] Rotationally restricted biaryls and especially axially chiral binaphthalenes are the most frequently employed compounds in this context. Interestingly, compared to their importance, their direct stereoselective synthesis remains challenging, especially in case of unsymmetric substituted biaryls. Besides these most important atropisomers, axially chiral aromatic amides constitute a substance class of relevance, in particular in the field of medicinal chemistry.[81]

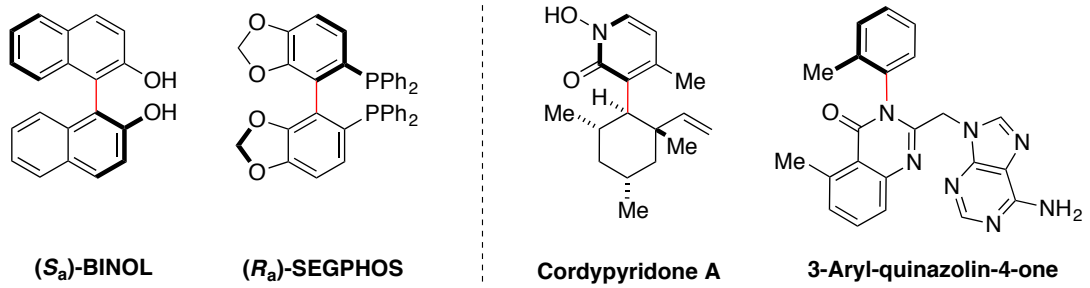


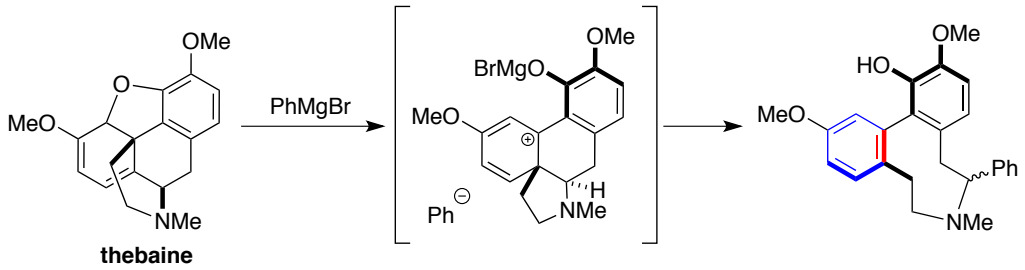
Figure 10: Two important axially chiral molecules employed as ligands in transition metal catalyzed stereoselective synthesis (left).[82] The bioactive natural product cordypyridone A[83] with an sp^2-sp^3-hybridized axially chiral C–C-bond and an axially chiral aromatic amide[84] representing a substance class important in medicinal (right).

Two conceptionally different strategies can be distinguished in the field of arene-forming atroposelective syntheses according to the source of stereoinduction: The substrate-stereocontrolled and the catalyst-stereocontrolled methods.

Substrate Stereocontrol

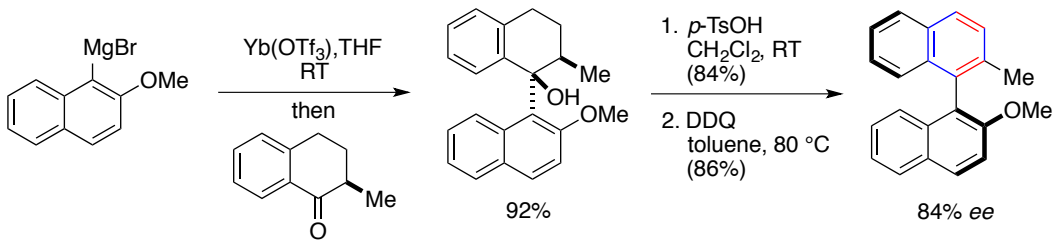
In a pioneering study, Berson discovered that the stereoselective formation of axially chiral biaryls can be realized by means of a central-to-axial chirality transfer (Scheme 28).[85] Treatment of the alkaloid thebaine with phenylmagnesium bromide resulted in a stereospecific arene-forming reaction giving the product as a mixture of two diastereoisomers that are solely different in the configuration of the sp^3-stereocenter. Berson assigned the absolute configuration of the stereogenic axis on the basis of the known configuration of

thebaine by considering the most likely pyrrolidine intermediate and proposed to utilize the obtained product as a standard to determine the configuration of other biaryls with polarimetry.[86] In the following years the subsequent advance of diffraction methods for structure elucidation revealed that minor modification in the substitution pattern of biaryls can influence the sense of optical rotation and X-ray crystallography became the method of choice to determine the absolute configuration of biaryls.



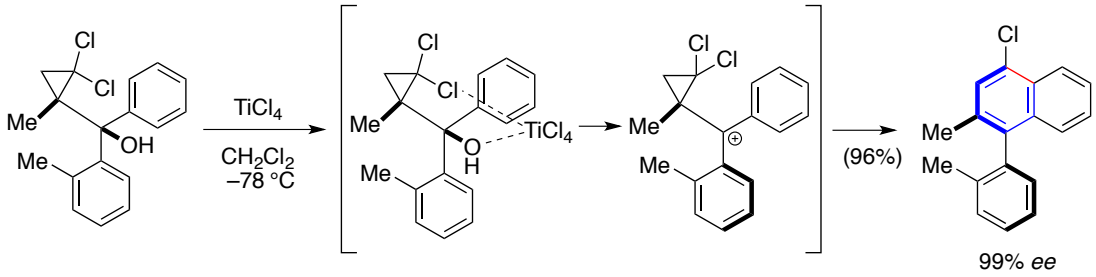
Scheme 28: Berson recognized the central-to-axial chirality transfer, when treating the natural product thebaine with PhMgBr.

The strategy to prepare axially chiral compounds starting from substrates with stereogenic carbon atoms has become a well-established methodology. The stereospecific transformation can either proceed during the aromatization step or in separate step as illustrated by the synthesis of tetra-*ortho*-substituted binaphthalenes reported by Miyano and coworkers (Scheme 29).[87] The transmetalation of 1-naphyl organomagnesium reagents to the corresponding ytterbium reagents allowed the 1,2-addition to enantiomerically pure (*R*)-2-methyl-1-tetralones, without competing α-deprotonation. The methyl group in α-position to the carbonyl effectively guides the attack of the nucleophile and provides a fully stereospecific conversion. The point-to-axial chirality conversion in the following by a *p*-TsOH induced 1,2-elimination and oxidation with DDQ delivered the optically active tetra-ortho-substituted binaphthalenes in excellent yields and with 84% enantiomeric excess.



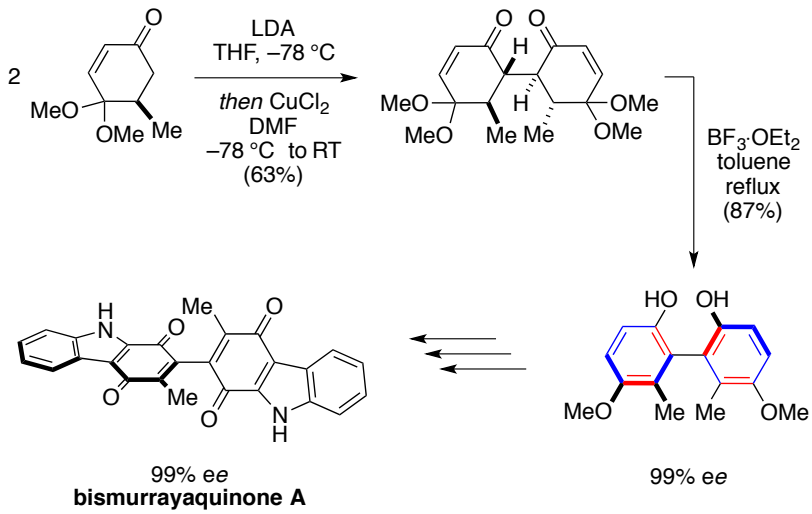
Scheme 29: Miyano's synthesis of tetra-*ortho*-substituted binaphthalenes by the addition of ytterbium reagents to enantiomerically pure (*R*)-2-methyl-1-tetralones followed by elimination and oxidation.

A strategy starting from enantioenriched gem-dichlorocyclopropanes giving direct stereospecific access to axially chiral biaryls without the need of additional dehydration and oxidations steps was reported by Nishii and Tanabe (Scheme 30).[88] Carbocation formation by dehydroxylation and an intramolecular Friedel-Crafts-type cyclization accompanied with cyclopropane-opening results in a Lewis acid induced arene forming 1,2-elimination of hydrogen chloride. In a single step the chiral information is effectively transferred from a sp^3 stereogenic center into the axially chiral scaffold. Steric repulsion between the methyl phenyl substituent and chelating $TiCl_4$ is proposed to be the reason for the high stereospecificity in the initial formation of the intermediary carbocation. The shortening of the C–C-bonds and planarization stabilize the new stereogenic axis of the intermediate and allow to obtain the desired aromatized products with high enantioselectivity and yields.



Scheme 30: A $TiCl_4$-induced Friedel-Crafts-type cyclization arene formation sequence transforms chiral *gem*-dihalocyclopropanes in unsymmetric substituted biaryls in extraordinary high efficiency.

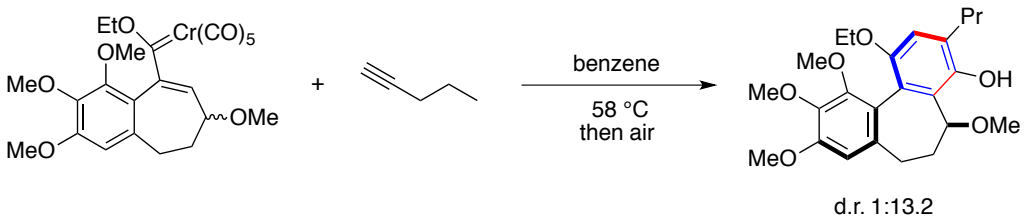
Thomson's total synthesis of bismurrayaquinone A demonstrates that the approach to transfer point into axial chirality in the context of aromatization reactions is not restricted to specifically designed starting materials (Scheme 31).[89] A fully stereospecific oxidative dimerization of an enantioenriched enone prepared by LDA deprotonation delivered the corresponding dione. BF_3•OEt_2 promoted aromatization in refluxing toluene allowed to efficiently transfer the stereochemical information and the desired bi-phenol was obtained in 87% yield with 99% enantiomeric excess. After four subsequent steps, bromination, amination, carbazole formation and oxidation, the desired natural product bismurrayaquinone A was obtained with high optical purity.



Scheme 31: Thomson's total synthesis of bismurrayaquinone A via oxidative dimerization and Lewis-acid induced stereospecific arene formation.

With the same strategy also various enones substituted with aryl-groups in β-position were dimerized and could be aromatized to give enantiomerically enriched and sterically crowded *ortho*-quarterphenyls.[90]

Investigations by Wulff and coworkers showed that chiral Fischer carbene complexes can be stereospecifically benzannulated with alkynes to give axially chiral biaryls (Scheme 32).[91] A racemic α,β-unsaturated chromium carbene complex was reacted with 1-pentyne to give an axially chiral biaryl with high diastereoselectivity by oxidative demetalation in air.



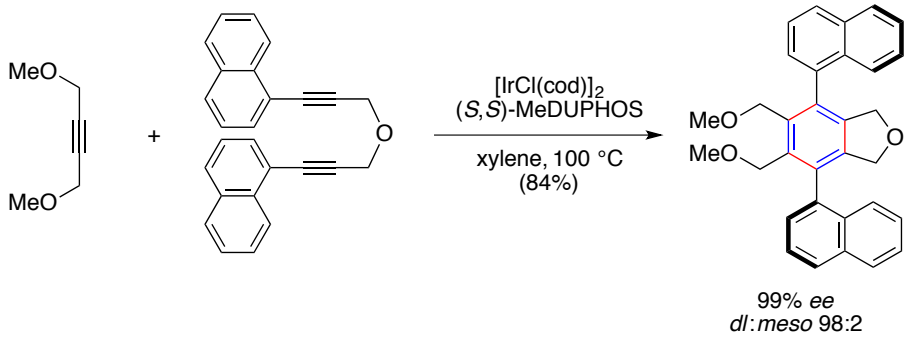
Scheme 32: Stereospecific central-to-axial chirality transfer benzannulation of a racemic Fischer-carbene complex reported by Wulff and coworkers.

Even though the substrate-controlled strategy, i.e. the preparation of axially chiral products via central-to-axial chirality transfer allows to prepare selectively one diastereoisomer over the other, the synthesis of non-racemic compounds by this approach requires an efficient access to the enantioenriched precursors. Consequently, methods with catalyst-controlled stereoinduction are very

appealing and various catalytic atroposelective arene-forming reactions have been developed.

Catalyst Stereocontrol

The catalyst-controlled [2+2+2]-cycloaddition is one of the most prominent methods to prepare axially chiral compounds in the context of the stereoselective arene-forming synthesis. In their remarkable investigations, Shibata and coworkers utilized a [2+2+2]-cycloaddition for the de novo construction of a central aromatic ring, simultaneously controlling the stereoselective formation of two rotationally restricted bonds giving axially chiral *p*-teraryls in one step (Scheme 33).[92] The symmetry breaking in the arene forming step allows a straightforward precursor synthesis, profiting from a bidirectional approach. The arene-forming reaction afforded the desired *p*-teraryls in good yields and with extraordinary enantiopurities employing 0.5 mol% of an iridium catalyst and the chiral phospine ligand MeDUPHOS.

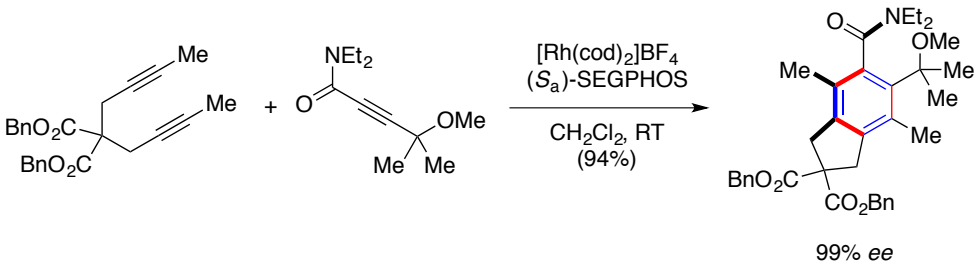


Scheme 33: Simultaneous stereocontrol in the formation of two axially chiral bonds in Shibata's [2+2+2]-cycloaddition approach to prepare axially chiral teraryls.

Intriguingly, Shibata further expanded his approach to form higher axially chiral biaryls.[93] The reaction of tetraynes and octaynes allowed to establish four and eight rotationally restricted bonds giving axially chiral polyaryls with excellent atroposelectivity. Nevertheless, the individual stereocontrol about every single chiral hindered bond remains a challenge to be solved in future.

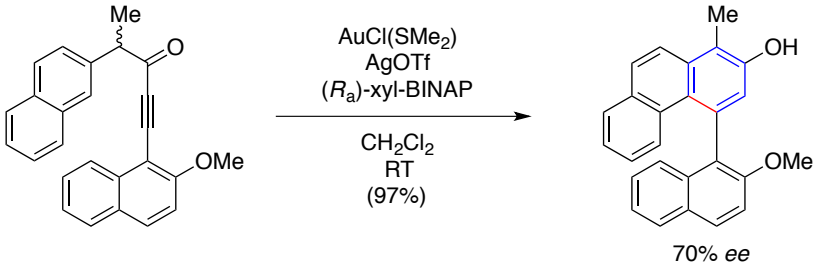
Apart from the synthesis of the well-known axially chiral biaryl scaffolds, the de novo construction of aromatic rings allows to selectively prepare atropisomeric aromatic amides, a substance class of growing significance in medicinal

chemistry.[81] Interestingly, depending on the substitution pattern aromatic amides are considered as multi axis systems, since the rotation can be hindered about the Ar–CO, the N–CO and also about the R–N bonds. Convenient catalyst controlled stereoselective methods complement traditional methods such as conglomerate crystallizations, kinetic resolutions or the use of stoichiometric chiral substrates or reagents. The improved accessibility enables to study the individually rotational behavior of these exceptional atropisomeric compounds. In seminal studies, Tanaka developed a rhodium-catalyzed atroposelective [2+2+2]-cycloaddition to prepare axially chiral amides.[94] The reaction of *N*,*N*-dialkylalkynylamides with 1,6-diynes provided highly substituted benzamides with restricted rotation about the aryl-carbonyl bond (Scheme 34). With the phosphine ligand (S_a)-SEGPHOS exquisite yields and excellent enantioselectivities could be realized.



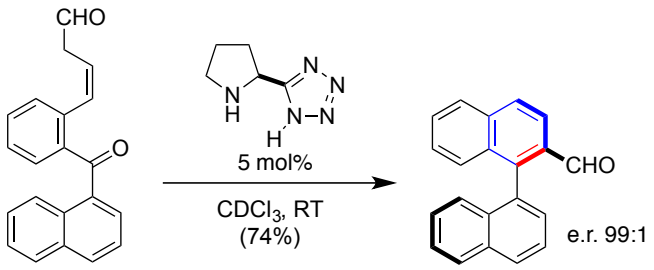
Scheme 34: Rh-catalyzed [2+2+2]-cycloaddition yielding sterically highly encumbered axially chiral amides.

The [2+2+2]-cycloadditions require two interlinked alkynes to ensure chemoselectivity, leading to the formation of a second ring vicinally connected to the new aromatic system. A gold-catalyzed atroposelective arene-forming intramolecular cycloisomerization reported by Tanaka allows the alkynone to react with a neighboring aromatic ring system leading to its extension (Scheme 35).[95] Racemic propargylic alcohols react to axially chiral phenanthrenes in an intramolecular arene-forming hydroarylation. The method affords non-symmetric biaryls in great yields and atroposelectivities up to 70% enantiomeric excess.



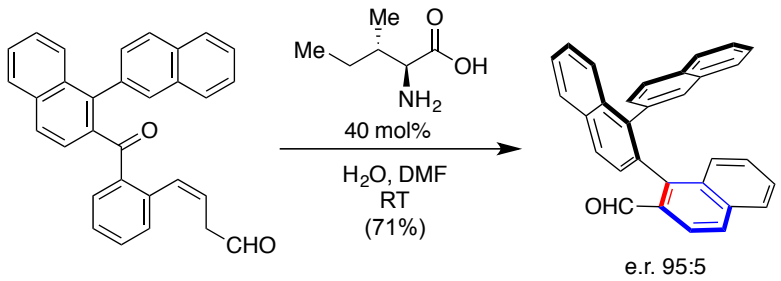
Scheme 35: Synthesis of enantioenriched axially chiral phenanthrenes by an Au-catalyzed intramolecular stereoselective arene-forming hydroarylation.

The catalyst-controlled stereoselective synthesis of axially chiral compounds usually depends on expensive transition metals such as palladium, iridium, rhodium or gold. Despite the fact that for the synthesis of highly valuable products with low catalyst loadings the price of the metal might be of secondary importance, the use of toxic transition metals is critical in the synthesis of pharmaceutical ingredients. The removal of these transition metals to the required levels can be very laborious and cost intensive. Therefore, catalysis by small organic molecules is highly desirable from an economic and ecological point of view. Inspired by the biosynthesis of natural aromatic polyketides and based on well-established stereoselective aldol methodology, our group developed an organocatalytic atroposelective aldol condensation.[96] Under mild conditions, unsymmetrical substituted axially chiral binaphthalene carbaldehydes could be synthesized by arene formation (Scheme 36).[97] The unsaturated ketoaldehyde substrates, readily accessible in a 4-step synthesis, are activated with 5 mol% of a commercially available pyrrolidinyl-tetrazole catalyst. The activated enamine intermediates undergo an intramolecular and highly stereoselective aldol addition, which is followed by a direct arene-forming aldol condensation. The non-symmetric binaphthalene aldehydes are obtained in good yields and with atroposelectivities of up to 99:1.



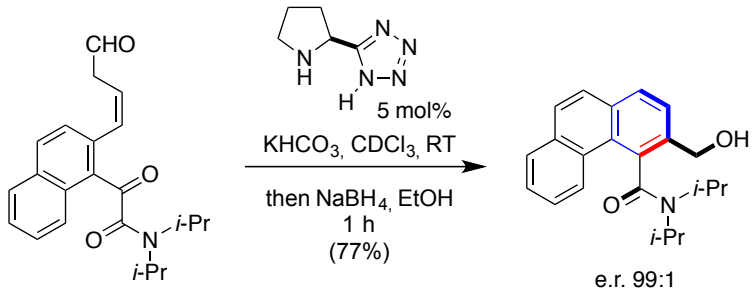
Scheme 36: Organocatalyzed stereoselective synthesis of axially chiral binaphthalene-2-carbaldehydes by an arene-forming aldol condensation

The ability to built up molecules with full control about the spatial arrangement of several connected molecular entities by govern multiple stereogenic axis is highly desirable. It enables to study structure-function relationships, which provides the opportunity to design and prepare materials with interesting optical, electronical or mechanical properties in the context bottom-up syntheses of functional systems. Based on the previously developed atroposelective arene-forming aldol condensation, our group investigated an approach to prepare the individual stereoisomers of *ortho*-arylene oligomers (Scheme 37).[98] The synthesis of structurally well-defined oligo-1,2-naphthylenes was achieved by the consecutive addition of an organometallic building block and iterative catalyst-controlled atroposelective arene-forming aldol condensations. In contrast to the related and also helically shaped, but configurationally dynamic *ortho*-phenylenes, the introduction of the third *ortho*-substituent leads to stable stereoisomers with high stereoisomerization barriers ($\Delta G^{\ddagger}_{453K}$= 154 kJmol^{-1} for the ternaphthalene).



Scheme 37: L-Leucin catalyzed stereoselective arene-forming aldol condensation to access *oligo*-1,2-naphthylenes.

Furthermore, the organocatalytic arene-forming aldol condensation was utilized to prepare axially chiral amides (Scheme 38).[99] *Ortho*-substituted arylglyoxylic amides could be rapidly converted under secondary amine catalysis to give axially chiral aromatic amides. A notable efficient aldol condensation was followed by an in situ reduction of the intermediary carbaldehydes, which increased the rotational barriers about the Ar–CO bond.



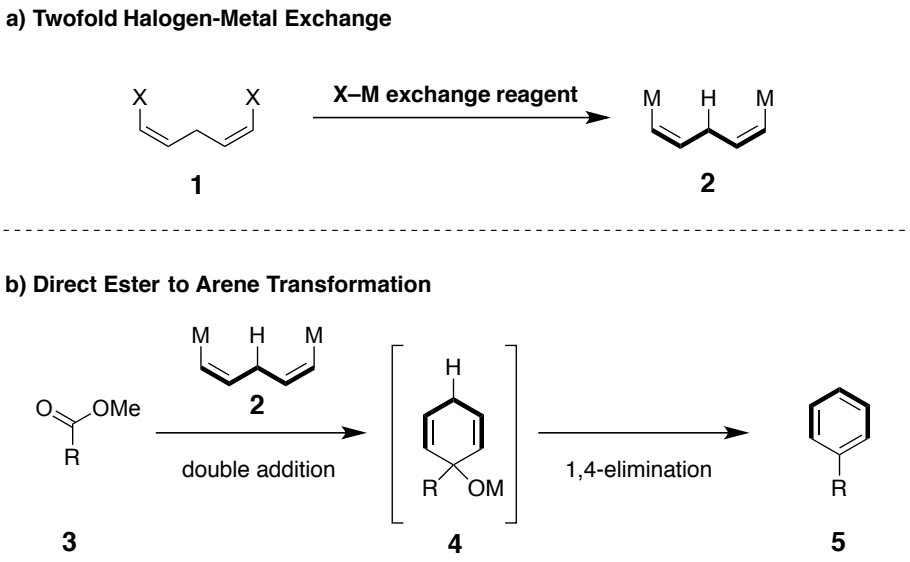
Scheme 38: Synthesis of axially chiral aromatic amides by a secondary amine catalyzed stereoselective arene-forming aldol condensation reduction sequence.

The presented examples of amine organocatalysis complement the transition metal catalyzed methods to prepare axially chiral compounds in the context of stereoselective arene-forming reactions. Apart from the catalytic strategies, the substrate-controlled methods starting from easy accessible chiral precursors by means of stereospecific central to axial chirality transfers often directly coupled with arene-formation is a feasible strategy.

2 Results and Discussion

2.1 Direct Transformation of Esters into Benzenes

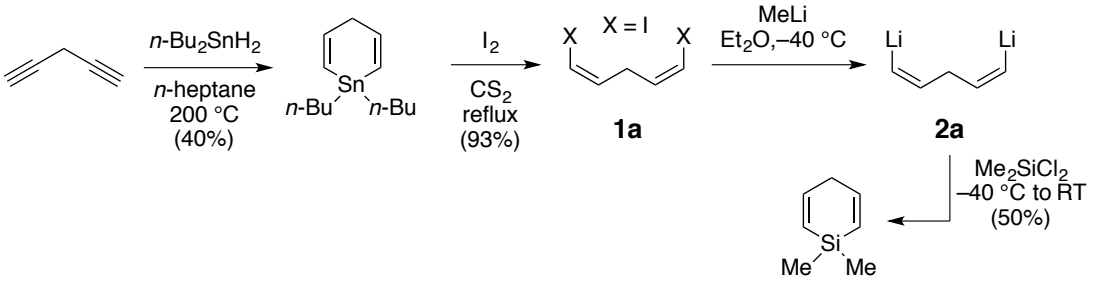
Considering the notable progress to access organometallic compounds by mild halogen-metal exchange procedures and the opportunity to add 1,5-bifunctional organometallic reagents to carboxylic acid esters as already described by Viktor Grignard in the early 20th century,[72] we envisioned to develop a double-halogen metal exchange of (1*Z*,4*Z*)-1,5-dihalopenta-1,4-diene **1** with a halogen-metal exchange reagent to give a 1,5-bifunctional organometallic reagent with retention of double bond configuration (Scheme 39). The double addition of reagent **2** to a carboxylic acid ester would deliver an intermediary cyclohexa-2,5-dienolate **4**, which then will be directly converted into an benzene **5** *via* a 1,4-elimination reaction. Expected challenges for the formation of dimetalla-1,4-pentadiene **2** are the considerable accumulation of electron density in the small pentadiene system, as well as the probability to metalate the "double" allylic position by deprotonation. Furthermore, the isomerization of the metalated olefin might complicate a successful reagent preparation and its subsequent application.



Scheme 39: a) A double halogen-metal exchange on **1** with a halogen-metal exchange reagent gives rise to (1*Z*,4*Z*)-1,5-dimetalla-1,4-pentadiene **2**. b) Direct ester to arene transformation by the double addition of 1,5-bifunctional organometallic reagent **2** to a carboxylic acid ester **3** followed by a 1,4-elimination to give access to arene **5**.

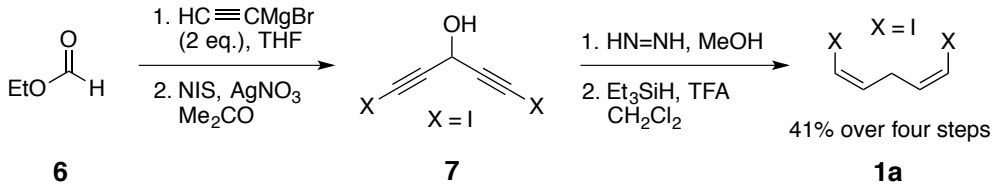
2.1.1 Preparation of Reagent-Precursor (1*Z*,4*Z*)-1,5-Diiodopenta-1,4-diene

The preparation of (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene **1a** from 1,1-dibutyl-1-stanna-2,5-cyclohexadiene was previously described by Jutzi and coworkers (Scheme 40).[100] The tin compound was obtained by double hydrostannylation of the labile diethynylmethane with dibutylstannane.[101] Treatment with iodine in CS_2 furnished diiodide **1a**, which was subjected to a two-fold iodine-lithium exchange with *n*-BuLi or MeLi at –40 °C. It was demonstrated that the highly reactive (1*Z*,4*Z*)-1,5-dilithiumpenta-1,4-diene (**2a**)[102] is capable to undergo a ring closing reaction by its direct double nucleophilic addition to dichlorodimethylsilane.



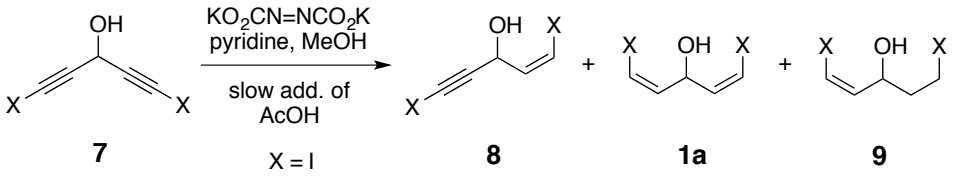
Scheme 40: Jutzi's synthesis of (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene (**1a**) followed by metalation with MeLi giving the corresponding di-lithium organyl **2a** and its direct reaction with dichlorodimethylsilane.

The findings by Jutzi showed that a dimetalla-compound like **2a** can be indeed prepared by a halogen-metal exchange and that it shows an adequate stability and reactivity. This encouraged us to prepare and investigate corresponding diorganomagnesium reagents. The project commenced by developing a tin-free synthesis of the desired (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene (**1a**), which after a double halogen-metal exchange would allow a direct ester to benzene transformation. A two-fold nucleophilic addition of commercially available ethynylmagnesium bromide solution to a solution of ethyl formate **6** in THF[103] and a following silver catalyzed di-iodination with *N*-iodosuccinimide in acetone[104] gave 1,5-diiodo-penta-1,4-diyn-3-ol (**7**) in a yield of 93%.



Scheme 41: Preparation of (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene (**1a**)

Subsequently, a (*Z*)-selective double iodo-alkyne reduction with diimide, in situ prepared by the acid induced decarboxylation of potassium azodicarboxylate, was developed (Scheme 42).[105] Aside of the desired double-reduction to the *cis*-diene **1a**, reduction of one alkyne (*mono*-reduction) to **8**, as well as concurrent over-reduction to the corresponding alkyl **9** was observed.



Scheme 42: Observed products in the diimide reduction of 1,5-diiodo-penta-1,4-diyn-3-ol (**7**).

The optimization proved to be challenging, since next to factors including temperature, concentration and equivalents of the diimide precursor, also the scale and presumably the stirring speed of the reaction have a significant influence on the ratio of the reaction products. The scale dependence was further recognized during *aqueous* workup with HCl (5%), since quenching the required excess of potassium azodicarboxylate led to diimide formation and therefore to further reduction, which was not observed in small scale nor while monitoring the reaction. These circumstances hampered effective reaction optimization. Most productive conditions were found at a scale of 45 mmol of diyne **7** and at a starting concentration of 0.75 molL^{-1} in MeOH. The diimide was formed in situ by slow addition of glacial acetic acid with a syringe pump to a solution of the substrate **7**, pyridine and potassium azodicarboxylate, while maintaining the reaction at room temperature. Purification by column chromatography was not successful at this stage. Therefore, the following dehydroxylation was conducted by adding triethylsilane to a solution of the crude reduction product mixture in trifluoroacetic acid.[106] The desired (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene (**1a**) was

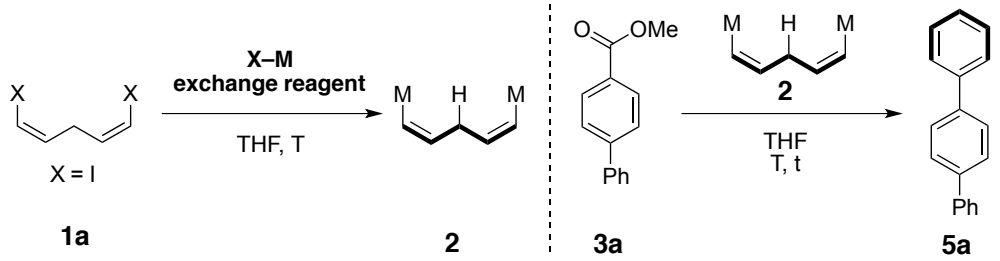
isolated in a yield of 41% over all four steps after purification by column chromatography. The individual fractions were analyzed by GC-MS, since the product is not UV-active and TLC-staining was unsuccessful.

It is pertinent to note that the corresponding (1*Z*,4*Z*)-1,5-dibromopenta-1,4-diene (**1b**, X=Br) prepared the same strategy, did not undergo metalation in several experiments with *n*-BuLi and elemental magnesium under various conditions.

2.1.2 Preparation of the Reagent (1*Z*,4*Z*)-1,5-Dimetallapenta-1,4-diene and Optimization of the Direct Ester to Benzene Transformation

With the required precursor **1a** in hand, conditions for the two-fold halogen-metal exchange followed by the direct double addition to an ester were investigated (Table 1). As a model substrate methyl 4-phenylbenzoate (**3a**) was chosen, due to the fact that the resulting *para*-terphenyl (**5a**) does not sublime at the reduced pressure during solvent evaporation at 40 °C, which is the case for most of the corresponding biphenyls.

Table 1: In situ generation of the reagent (1*Z*,4*Z*)-1,5-dimetallapenta-1,4-diene (**2**)[a] and optimization of the reaction parameters of the direct ester to benzene transformation.[b]



Entry	X–M Exchange Reagent	T	t	Yield[c]
1[d]	*n*-BuLi	–40 °C	2 h	46%
2[e]	*i*-Pr*n*-Bu$_2$MgLi	0 °C	30 min	70%
3	*i*-Pr*n*-Bu$_2$MgLi	0 °C	30 min	70%
4	*n*-Bu$_3$MgLi	0 °C	30 min	64%
5	*s*-Bu*n*-Bu$_2$MgLi	0 °C	30 min	56%
6	*i*-Pr*n*-Bu$_2$MgLi	–20 °C	30 min	69%
7	***i*-Pr*n*-Bu$_2$MgLi**	**–20 °C**	**2 h**	**82%**
8	*i*-Pr*n*-Bu$_2$MgLi	–40 °C	2 h	61%
9[f]	*i*-Pr*n*-Bu$_2$MgLi	–20 °C	2 h	70%
10[g]	*i*-Pr*n*-Bu$_2$MgLi	–20 °C	2 h	73%

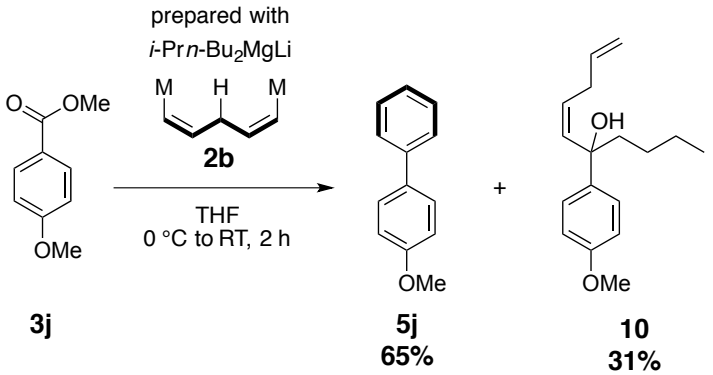
[a] Reactions performed with 200 µmol (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene (**1a**) and 200 µmol X-M exchange reagent for 5 min at temperature (T). [b] 100 µmol methyl 4-phenylbenzoate (**3a**) and in situ generated (1*Z*,4*Z*)-1,5-dimetallapenta-1,4-diene (**2**) for the time (t) at the temperature (T) followed by aqueous work-up (HCl 1.0 molL^{-1}). [c] Yield of isolated product *para*-terphenyl (**5a**). [d] Reaction was performed in Et$_2$O. [e] Purchased from Sigma-Aldrich, No. 683418. [f] (1*Z*,4*Z*)-1,5-dimetallapenta-1,4-diene (**2**) was kept 2 h at –20 °C prior the reaction with methyl 4-phenylbenzoate (**3a**). [g] 160 µmol (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene (**1a**) and 160 µmol X-M exchange reagent.

Initial, halogen-metal exchange under the conditions described by Jutzi[100] at –40 °C in Et_2O with *n*-BuLi followed by direct in situ addition of the bifunctional (1*Z*,4*Z*)-1,5-dilithiumpenta-1,4-diene (**2a**) to ester **3a** gave the desired aromatized product **5a** after workup with one molar *aqueous* hydrochloric acid in an encouraging yield of 46% (Table 1, entry 1). Transmetalation of the di-lithium reagent **2a** with MgX_2[107] to form the corresponding Grignard reagent did not yield any product after the ester addition. The direct metalation of the diiodo-reagent-precursor **1a** with elemental magnesium[108] was not successful and even after heating for several hours, no reagent formation was accomplished. Therefore, the halogen-metal exchange reagent *i*-PrMgCl•LiCl ("Turbo-Grignard"),[27] known for its capability to prepare alkenylmagnesium reagents by halogen-metal exchange with alkenyl iodides,[34] was employed. However, even after prolonged reaction times, by heating and using an excess of *i*-PrMgCl•LiCl, only partial mono-metalation was observed. Our attention was then turned to *s*-Bu_2Mg•LiCl, which shows an increased magnesiate character[21] compared to the "Turbo-Grignard" reagent and is prepared by adding one equivalent of *s*-BuLi to one equivalent *s*-BuMgCl in THF at room temperature. The obtained *s*-Bu_2Mg•LiCl allowed to achieve complete halogen-metal exchange in 2 h with diiodo-reagent-precursor **1a** in the 1- and 5-position at room temperature, however the resulting reagent did not convert the carboxylic acid ester **3a** to the desired arene **5a**. Next, (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene (**1a**) was treated with the commercially available heteroleptic magnesiate *i*-Pr*n*-Bu_2MgLi (Table 1, entry 2).[41] Already after 5 min at 0 °C the halogen-metal exchange was complete. Ester addition and stirring for 30 min gave, after acidic workup the desired *para*-terphenyl (**5a**) in a promising yield of 70%. Alternatively, the employed magnesiate *i*-Pr*n*-Bu_2MgLi can readily prepared by mixing one equivalent *i*-PrMgCl and two equivalents *n*-BuLi (Table 1, entry 3). Furthermore, the reaction was carried out with the magnesiates *n*-Bu_3MgLi and *s*-Bu*n*-Bu_2MgLi to find *i*-Pr*n*-Bu_2MgLi as the superior halogen-metal exchange reagent (Table 1, entries 4 and 5 versus entry 3). A considerable increase in yield was achieved after optimization of the reaction time and temperature. It further turned out that the immediate use of the in situ prepared organometallic reagent **2b**, as well as the employment of an excess of the

reagent was necessary to compensate decomposition pathways and increase the yield of the desired *para*-terphenyl (**5a**) to 82%.

Based on the observation that except of the highly reactive dilithium species **2a** and the more efficient magnesiate species **2b**, non of the prepared reagents reacted with the ester group, it can be assumed that the magnesiate character and reactivity trends of the exchange reagent *i*-Pr*n*-Bu_2MgLi is largely transferred to the bifunctional organomagnesiate reagents. Furthermore, the higher yields achieved with the bifunctional magnesiates compared to the labile dilithium reagent **2a** could be attributed to its higher stability and matching reactivity for the desired reaction.

Interestingly, tertiary alcohol **10** could be found as a major side product in the reaction of bifunctional organometallic reagent **2b** with methyl anisate **3j**. It is reasonable to assume that this side product is formed by the intramolecular attack a *n*-butyl-group carried by the magnesiate, which is competing with the attack of the alkenyl-residue.

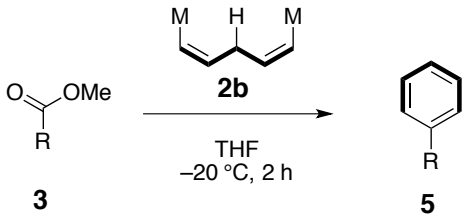


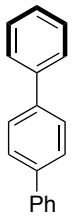
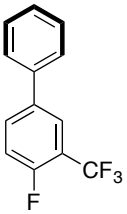
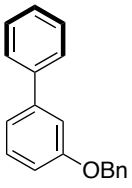
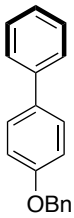
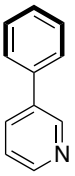
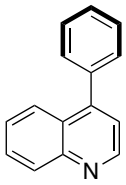
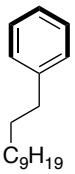
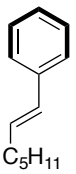
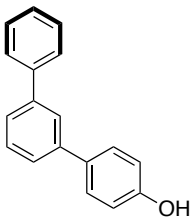
Scheme 43: Observation of the formation of side product **10**. Conversion determined by ^{1}H-NMR spectroscopy with the internal standard durene.

2.1.3 Substrate Scope of the Direct Ester to Benzene Transformation

After successful optimization of the reaction conditions the scope of the direct ester to benzene transformation was explored. Esters with electron deficient groups reacted with comparable efficiency (Table 2, entry 2). In contrast esters with electron-donating groups proved to be less reactive, which became evident by lower yields (Table 2, entries 3 and 4). The *N*-heterocyclic carboxylic acid ester methyl nicotinate **3e** reacted to the desired biphenyl **5e** in higher yield (Table 2, entry 5). Also the 4-phenyl-substituted quinoline derivative **3f**, with its *ortho*-substitution more sterically demanding, was obtained effectively (Table 2, entry 6). Besides the phenyl-substituted substrates, even alkyl and alkenyl esters gave access to the corresponding benzene derivatives **5g** and **5h** in synthetically meaningful yields (Table 2, entry 7 and 8), which emphasizes the general scope of the method. Also an ester carrying a protic group was converted successfully by employing an additional equivalent of the 1,5-bifunctional organomagnesium reagent **2b** to give *meta*-terphenyl **5i** in a yield of 80% (Table 2,entry 9).

Table 2: Substrate scope of the direct ester to benzene transformation employing 1,5-bifunctional organomagnesiate reagent **2b**.[a]



Entry	Product[b]	Entry	Product[b]	Entry	Product[b]
1		2		3	
	5a, 82%		**5b**, 80%		**5c**, 59%
4		5		6	
	5d, 57%		**5e**, 72%		**5f**, 68%
7		8		9	
	5g, 68%		**5h**, 60%		**5i**, 80%

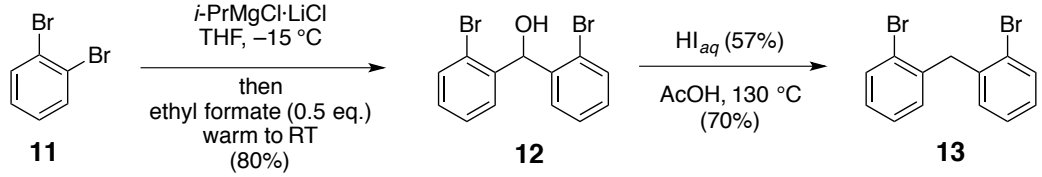
[a] Reactions performed with 100 µmol ester **3** and in situ prepared magnesiate **2b** (from 200 µmol **1a** and 200 µmol *i*-Pr*n*-Bu$_2$MgLi) at –20 °C for 2 h, followed by *aqueous* workup with HCl 1 molL^{-1} [b] Yields of isolated products. [c] prepared with **2b** from 300 µmol **1a** and 300 µmol *i*-Pr*n*-Bu$_2$MgLi.

2.2 Direct Transformation of Esters into Anthracenes

After the successful development of the direct transformation of carboxylic acid esters into benzene derivatives, the scope of the strategy was expanded by developing a 1,5-bifunctional organomagnesium reagent amenable for the direct transformation of esters into anthracene derivatives.

2.2.1 Preparation of Reagent Precursor Bis(2-bromophenyl)methane

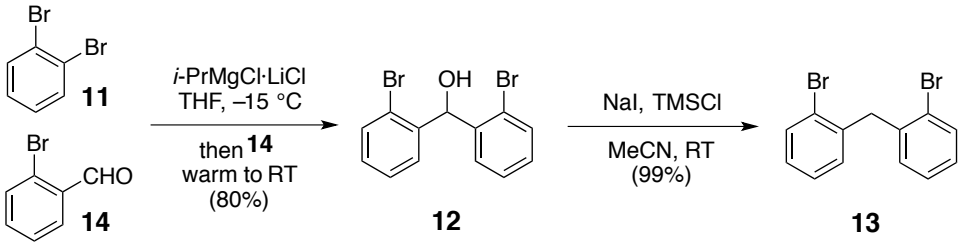
The first approach of the reagent-precursor synthesis started with a LiCl-promoted mono-Br–Mg exchange of 1,2-dibromobenzene (**11**) as described by Knochel (Scheme 44).[27] Aryne formation from the intermediary *ortho*-bromophenylmagnesiumchlorid LiCl was successfully prevented by the relatively low temperature of –15 °C. Addition of ethyl formate and slow warm-up to room temperature gave access to bis(2-bromophenyl)methanol (**12**) in 80% yield. Subsequent dehydroxylation in acetic acid with concentrated hydroiodic acid at 130 °C gave the desired reagent precursor in a yield of 70%. The overall synthetic pathway followed the strategy described by Piers and coworkers, who prepared the desired bis(2-bromophenyl)methane (**13**) starting from 2-bromoiodobenzene.[109]



Scheme 44: First generation synthesis of reagent-precursor bis(2-bromophenyl)methane (**13**).

In the further course of the project, a more scalable, cost-efficient and column-chromatography-free synthesis was developed (Scheme 45). Applying 2-bromobenzaldehyde (**14**) as the electrophile in the first reaction is more cost-effective, since it allows to halve the required amount of "Turbo-Grignard"-reagent and to conduct the reaction at higher concentration. After recrystallization 116 g (80%) of bis(2-bromophenyl)methanol (**12**) was obtained. A TMSI-mediated reduction method allowed to conduct the dehydroxylation with full conversion at room temperature and at high concentration in MeCN.[110] By

this, the tedious workup after the first generation dehydroxylation reaction with the necessity to neutralize large amounts of the acidic reaction mixture was circumvented. Finally, removing traces of iodine by high-vacuum evaporation delivered the desired product **13** as a clear, yellow liquid.



Scheme 45: Second generation synthesis: More efficient route and scale up of the synthesis of reagent-precursor **13**.

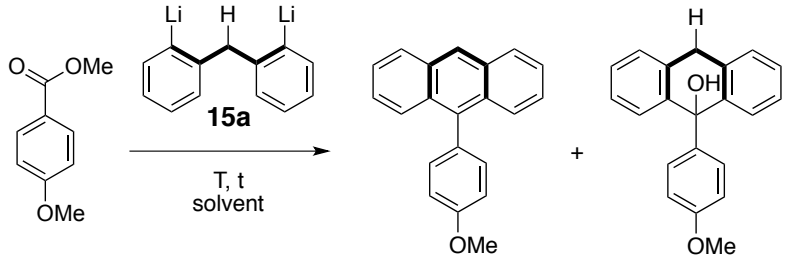
2.2.2 Reagent Preparation, Optimization of the Ester to Anthracene Transformation and Observed Salt Effects

In preliminary experiments *n*-BuLi was added to a solution of *o*,*o*'-dibromoaryl-methane **13** in Et_2O at room temperature and the reaction was stirred for 5 min. Then the mixture was portioned and added to separate solutions of ethyl formate, ethyl acetate and methyl benzoate. After stirring for 10 min at room temperature the reaction mixtures were quenched with a small amount of water, all solvents were evaporated under reduced pressure and the NMR spectra of the crude reaction mixtures were recorded. Traces of the corresponding anthracene product could be identified by comparing the characteristic shifts of the 9-H-anthracene-peaks with the literature-known ^{1}H-NMR-spectra. Furthermore, the completeness of the X–M-exchange could be observed.

Next, the non-volatile and crystalline ester methyl anisate (**3j**) was chosen as a model substrate to further investigate the reaction. The reaction with the 1,5-bifunctional organolithium-reagent **15a** at –78 °C in Et_2O allowed, after workup with H_2O, to isolate the desired anthracene product **16a** in 3% yield and a decent amount of 59% of the corresponding tertiary alcohol **17a** (Table 3, entry 1). Conducting the reaction in THF and allowing the reaction to warm up to room temperature increased the yield of aromatized product **16a** (Table 3, entry 2). Adding *N*,*N*,*N*',*N*'-*tetra*-methylenediamine (TMEDA) as well as running the reaction in *n*-hexane did not improve the reaction outcome (Table 3, entry 3 and

4). Recognizing the high reactivity of the dilithium-compound **15a** we aimed to prepare the corresponding organomagnesium-species by X–M-exchange with *i*-PrMgCl•LiCl. However after stirring for 24 h in THF at room temperature, halogen-metal exchange was incomplete and after quenching with water, only the formation of traces of diphenylmethane was observed (Table 3, entry 5).

Table 3: Initial screening experiments for the direct ester to anthracene transformation employing the 1,5-bifunctioal organolithium-reagent **15a**.[a]



3j **16a** **17a**

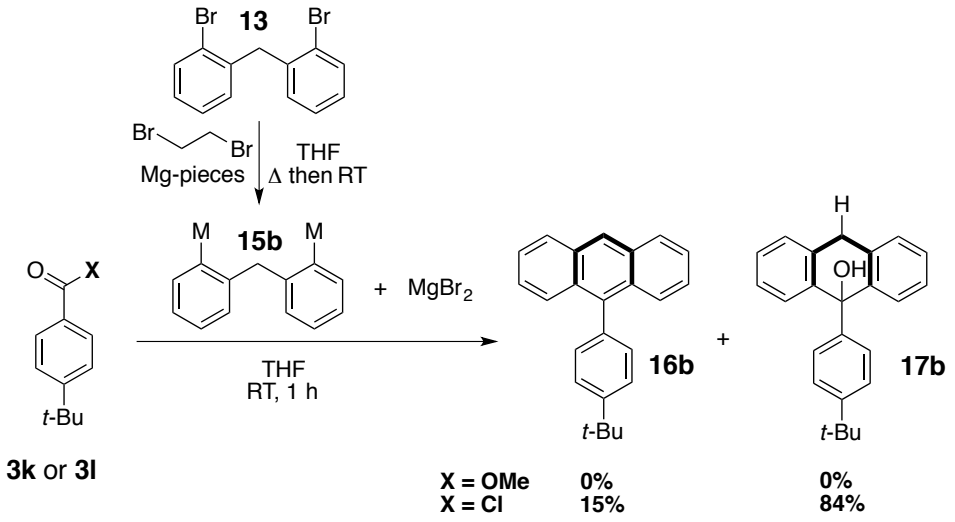
Entry[b]	T	t	solvent	Yield of **16a**[c]	Yield of **17a**[c]
1	–78 °C	1 h	Et_2O	3%	59%
2	–78 °C to RT	3 h	THF	11%	45%
3[d]	–78 °C to RT	1 h	THF	—	traces
4[e]	RT	0.5 h	*n*-hexane	6%	36%
5[f]	RT	24 h	THF	—	—

[a] Reactions performed with 100 µmol methyl anisate (**3j**) and 1,5-diorganolithium-reagent **15a** derived from 200 µmol of bis(2-bromophenyl)methane (**13**). Not titrated. [b] at T for t followed by aqueous workup with H_2O. [c] Yield of isolated products. [d] addition of 225 µmol TMEDA [e] X–M-Exchange in Et_2O, evaporation of solvent under reduced pressure and wash of precipitate with *n*-hexane [f] use of a 1,5-bifunctional diorganomagnesium reagent prepared by X–M-Exchange with *i*-PrMgCl•LiCl.

The performed reactions proved the ability of the dilithium-reagent **15a** to undergo a double nucleophilic addition to an ester whereby small amounts of the aromatized compound could be isolated without acidic workup. Although the obtained major product turned out to be tertiary alcohol **17a**. Nevertheless, in the ^{1}H-NMR-spectra, always broad signals were observed, which presumably corresponded to partially insoluble side-products that did not elute during silica gel column chromatography, suggesting to be oligomeric or polymeric side products. Adding an aqueous HCl-solution (1 molL^{-1}) to a solution of pure **17a** in

THF and stirring for 5 min at room temperature gave the pure desired anthracene **16a** in quantitative yield.

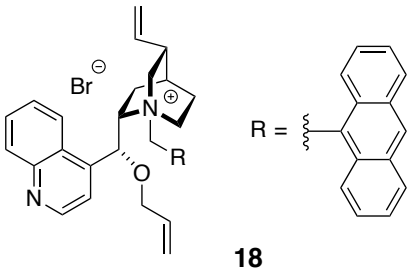
To increase the yield of the double nucleophilic addition the preparation of the less reactive corresponding 1,5-bifunctional organomagnesium reagent **15b** by direct metalation with elemental magnesium was investigated next. Piers and others already reported the formation of **15b** by a direct magnesiation of dibromo-precursor **13**, however the conditions for its formation were not described in detail.[109] Initial experiments to form **15b** were not successful. However, after activation of the at the surface passivated magnesium-pieces with the entrainment reagent 1,2-dibromoethane and starting the reaction by repeatedly heating the reaction solution to mild reflux, full metalation was observed within 1 h at room temperature.



Scheme 46: Two-fold magnesiation of bis(2-bromophenyl)methane to prepare the 1,5-bifunctinal organomagnesium reagent **15b** after activation of magnesium pieces by the entrainment reagent 1,2-dibromoethane and direct reaction with ester **3k** respectively the corresponding acid chloride **3l**.

The organomagnesium reagent **15b** was added to ester **3k**, but no reaction was observed. Intriguingly, addition of the more electrophilic corresponding acyl chloride gave a combined yield of 99% of the desired products after workup with *aqueous* NH_4Cl-solution (see Scheme 46). This assured that the 1,5-bifunctional organomagnesium reagent indeed can be formed by direct magnesiation and also undergoes the double nucleophilic addition more efficiently than the corresponding dilithium-reagent **15a**. Nevertheless, its reactivity seemed to be

too low for the desired transformation of carboxylic acid ester substrates. Therefore, additives were screened to increase the reactivity of the 1,5-bifunctional organomagnesium reagent, respectively to activate the carboxylic acid ester substrates (Table 4). Another interesting aspect to investigate was, if an additive might induce or accelerate the aromatization and if this would allow for a mild acidic workup, not requiring treatment with hydrochloric acid. All the reactions were therefore quenched consistently with NH_4Cl-solution after 30 min and monitored by comparing the integrals of characteristic substrate and product peaks in the ^{1}H-NMR spectra. First, the commercially available lanthanide salt complex $LaCl_3$•2LiCl in THF, which is known for its ability to enhance 1,2-additions [111] was added and full conversion of the ester was observed within 30 min. Similar results were found with predried $CeCl_3$ (Table 4, entry 1 & 2). No product formation was observed with the Lewis acids $TiCl_3$ and $AlCl_3$ (Table 4, entries 3–6). The same was observed for $FeBr_3$ and $MgCl_2$, while employment of $MgBr_2$ led to low conversion (Table 4, entries 7–9). With pre-dried LiCl and $CaCl_2$ full conversion to tertiary alcohol **17b**, but no aromatization was monitored (Table 4, entries 10 & 11). One Equivalent of BF_3•OEt_2 led to a conversion of 72% to the tertiary alcohol, while with $B(OMe)_3$ a conversion of 28% was observed (Table 4, entries 12 & 13). Using *tetra*-*n*-butylammonium bromide (TBAB) as an additive gave also full conversion (Table 4, entry 14) . Most interestingly the amount of TBAB could be reduced to 10 mol% without loosing its ability to induce the reaction and allowed to isolate 89% of alcohol **17b** and 9% of anthracene **16a** (Table 4, entry 15). Next, various *tetra*-*n*-butylammonium salts were employed as additives in catalytic amounts to explore the influence of the counter-anion, however similar results were observed for all anions (Table 4 ,entries 16–20).



18

Figure 11: *O*-Allyl-*N*-(9-anthracenylmethyl)cinchonidinium bromide [200132-54-3] a cinchona-based chiral phase-transfer catalyst utilized as catalytic additive see **Table 4**, entry 21.

Intrigued by the possibility to catalyze a Grignard reaction at room temperature with an ammonium salt, we also tested the commercially available cinchona-based phase transfer catalyst **18** and observed partial conversion (Table 4, entry 21). This initial result opened up the opportunity to stereoselectively catalyze a reaction of a corresponding unsymmetric 1,5-bifunctional organomagnesium reagent with an non-symmetric ester giving enantioenriched axially chiral products (investigate further in chapter 2.7.2). For the current aim to transform esters into acenes, we concluded that the 1,2-addition could be induced successfully by several additives even in catalytic amounts, however none of the tested additives accelerated the aromatization process to a significant extent.

Table 4: Screening of additives in the reaction of ester **3k** with 1,5-bifunctional organomagnesium reagent **15b** shown in **Scheme 46**.[a]

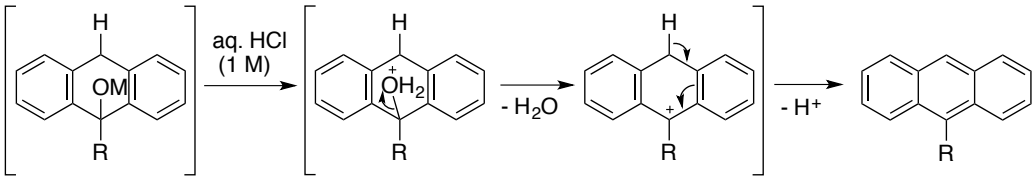
Entry	Additive[b]	Conversion to anthracene **16b**[c]	Conversion to alcohol **17b**[c]
1	$LaCl_3$•2LiCl	7%	93%
2	$CeCl_3$	7%	93%
3	$Ti(O\textit{i}\text{-}Pr)_4$	—	—
4	$TiCl_4$	—	—
5	$TiCl_4$, NEt_3	—	—
6	$AlCl_3$	—	—
7	$FeBr_3$	—	—
8	$MgCl_2$	—	—
9	$MgBr_2$	21%	23%
10	$CaCl_2$	—	100%
11	LiCl	—	100%
12	BF_3•OEt_2	—	72%
13	$B(OMe)_3$	—	28%
14	TBAB	6%	94%
15[e]	**TBAB**	**9%**[d]	**89%**[d]
16[f]	TBA-I	3%	97%
17[f]	TBA-Cl	1%	99%
18[f]	TBA-BH_4	4%	96%
19[f]	TBA-HSO_4	—	100%
20[f]	TBAF	—	73%
21[e]	**18**	**2 h**	**73%**

[a] Reactions performed with 100 µmol of ester **3k** and 200 µmol of 1,5-bifunctional organomagnesium reagent **15b** derived from 200 µmol of bis(2-bromophenyl)methane (**13**) after Mg activation with 2 drops of 1,2-dibromoethane. Not titrated. [b] 100 µmol of the specified additive, if not stated otherwise. [c] conversion calculated from the sum of integrals of substrate and product specific peaks in the ^{1}H-NMR of the crude reaction mixture after workup with *aq. sat.* NH_4Cl-solution. [d] isolated product after purification with column chromatography [e] 10 mol% of additive. [f] 20 mol% of additive.

In the further course of the project together with C. Fischer, it was recognized that cutting the magnesium into tiny pieces and heating them shortly under vacuum with the heat gun prior to solvent addition sufficiently activates the magnesium surface and allows to start the metalation without the need to use 1,2-dibromoethane. By this, no additional $MgBr_2$ is introduced into the reaction mixture and it was observed that after complete halogen–metal-exchange over 12 h at room temperature the resulting 1,5-bifunctional organomagnesium reagent **15b** is capable to react highly efficient with carboxylic acid esters to give, after aqueous acidic workup with hydrochloric acid (1 $molL^{-1}$), the desired anthracenes **16** in excellent yields (see next chapter 2.2.3).

Preliminary mechanistic insights into the 1,4-elimination

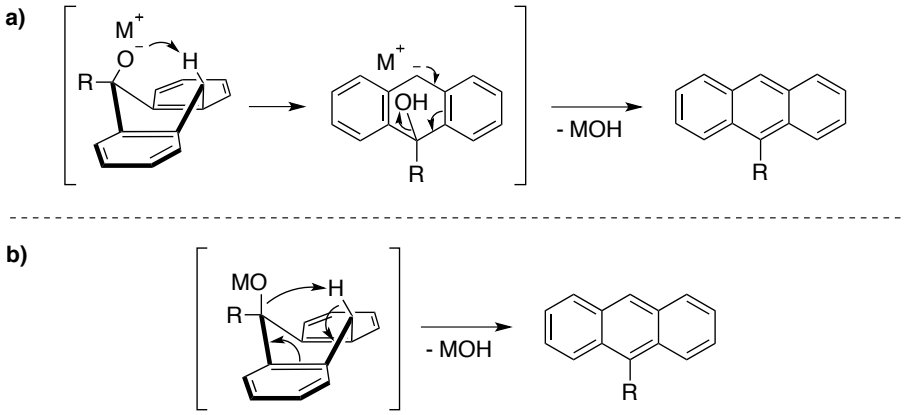
The experiments described above revealed that aqueous acidic workup with hydrochloric acid is necessary to achieve full aromatization of intermediary formed tertiary alkoxide. This is an indication for a step-wise i.e. an unimolecular elimination mechanism (E1) via the formation of a carbocation (Scheme 47).



Scheme 47: Proposed step-wise elimination mechanism for the hydrochloride acid induced aromatization of the intermediary alkoxide.

However, in all experiments that have been quenched with H_2O or aqueous saturated NH_4Cl-solution minor amounts (1% to 21%) of aromatized product have been observed (cf. Table 3, Scheme 46 and Table 4). The observed quantities changed depending on the organometallic reagent, ester, solvent and additives employed. The observation of the direct formation of aromatized products under basic conditions respectively mild acidic conditions might be explained by the mechanism described in the following. Assuming that the molecule can adopt a boat like conformation, the alkoxide anion could abstract a proton from the benzylic position (Scheme 48). The intramolecular relocation of the proton would lead to aromatization with a hydroxide as a leaving group. Though, the hydroxy-

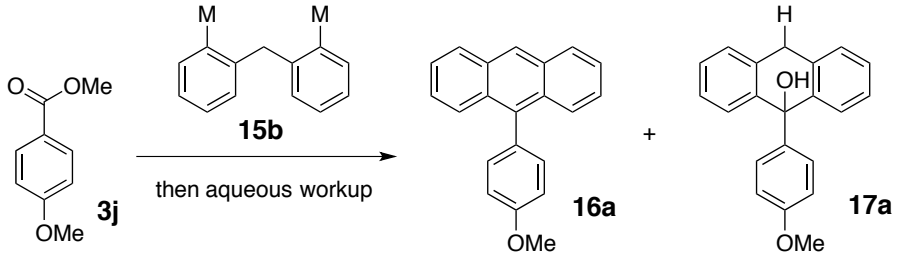
group is known to be a poor leaving group, its departure may be driven by the aromatization-process in this case and further supported by coordinating metal cations, which would stabilize its negative charge upon cleavage. Alternatively, the 1,4-elimination might occur via a concerted mechanism.



Scheme 48: Possible mechanisms of the direct intramolecular aromatization under basic conditions: a) stepwise or b) concerted.

A series of reactions were performed by C. Fischer to get an insight, if prolonged reaction times and higher temperatures influence the product distribution between directly formed aromatized product and tertiary alcohol (Table 5). When the reaction was conducted at 60 °C instead of at RT, an increased amount of aromatized product was found (Table 5, entry 1 and 2). Elongation of the reaction time also gave more anthracene product (Table 5, entry 3). This indicated that indeed the aromatization might happen already before aqueous workup. However, when the reaction was quenched with H_2O less than 1% of aromatized product could be isolated. Depending on the substrate and conditions, the 1,4-elimination takes place under the basic conditions and the acidic work-up in different extend.

Table 5: Influence of reaction temperature and time on the product distribution in the direct ester to anthracene transformation with 1,5-bifunctional organomagnesium reagent **15b** after aqueous workup.[1]



Entry	T	t	workup	ratio **16a** / **17a** [a]
1	RT	4 h	aq. sat NH_4Cl	12:88
2	60 °C	4 h	aq. sat NH_4Cl	19:81
3	60 °C	16 h	aq. sat NH_4Cl	27:73
4	RT	4 h	deion. H_2O	<1:99

[a] ratios of **16a** / **17a** determined by ^{1}H-NMR (**16a**: δ = 8.03 ppm; **17a**: δ = 7.86 ppm).

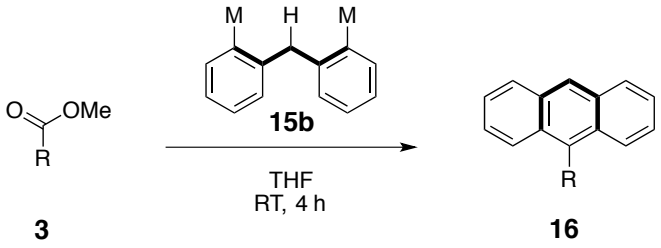
In contrast, the reaction of the 1,5-bifunctional organolithium reagent **15a** with the same ester **3j** gave more of the aromatized product also after workup with H_2O (see Table 3). This result supports that also a base induced aromatization process might be present.

[1] Investigations and reactions performed by Christian Fischer.

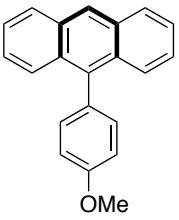
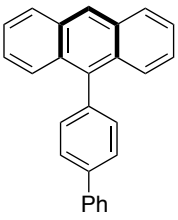
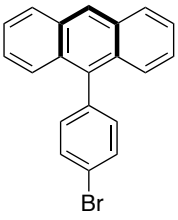
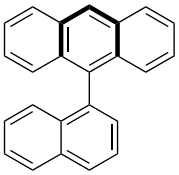
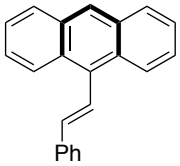
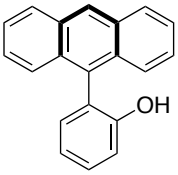
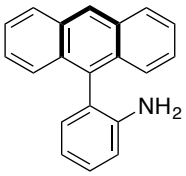
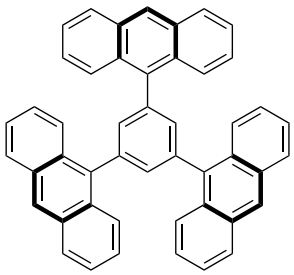
2.2.3 Substrate Scope of the Direct Ester to Anthracene Transformation

In contrast to the di-metalla-pentadiene reagent **2** utilized for the benzene synthesis, the 1,5-bifunctional arylic organomagnesium reagent **15b** was found to be stable at room temperature. Reagent **15b** reacted at room temperature with the electron-rich aryl-substituted carboxylic acid ester **3j** with exceptional efficiency to the desired biaryl product **16a** in 97% yield (Table 6, entry 1). The higher polarity of the product compared to the other products simplified purification by column chromatography and for this reason the potential to perform the direct ester to anthracene transformation on a preparative scale was investigated with this substrate (Table 6, entries 2 and 3, 1 mmol and 10 mmol). Next, methyl 4-phenyl benzoate (**3a**) was converted to give the corresponding anthracene **16c** in a remarkable yield of 99%. A bromo-substituted phenylanthracene, as well as a naphthylderivative with increased steric bulk were obtained in excellent yields (Table 6, entries 5 and 6). The broad substrate scope is exemplified by the effective preparation of the alkenyl derivative **16f** (Table 6, entry 7). By employing an access of Grignard reagent **15b**, also aryl esters carrying unprotected hydroxy- and amino-groups gave the corresponding anthracene derivatives in high yields (Table 6, entries 8 and 9). The capability to transform multiple ester groups in close proximity to each other is demonstrated by the threefold ester to arene transformation to give product **16i** in an yield of 55%, when the third aromatization is induced by treatment with concentrated *aqueous* hydrochloric acid in a separate step (Table 6, entry 10).

Table 6: Substrate scope of the direct ester to anthracene transformation employing 1,5-bifunctional organomagnesium reagent **13**.[2]



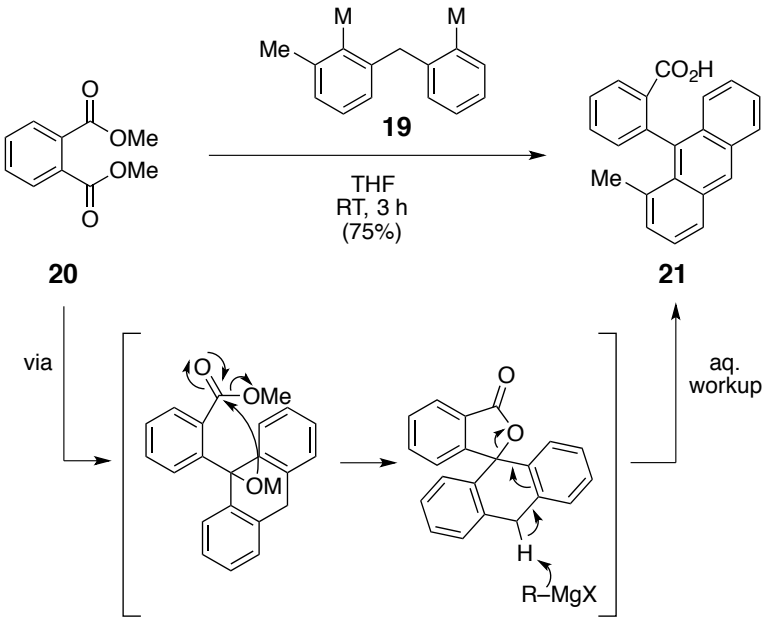
3 **16**

Entry[a]	Product[b]	Entry	Product[b]	Entry	Product[b]
1–3		2–4		5	
	16a, 97% 99%,[c] 94%[d]		**16c**, 99%		**16d**, 99%
6		7		8	
	16e, 97%		**16f**, 87%		**16g**, 88%[e]
9		10			
	16h, 99%[f]		**16i**, 55%[g]		

[a] Reactions performed with 100 µmol ester **3** in THF (1.0 mL) and 140 µmol **15b** at RT for 4 h, followed by *aqueous* workup with HCl 1 molL^{-1} [b] Yields of isolated products. [c] scale of 1.00 mmol. [d] scale of 10.0 mmol. [e] 200 µmol of **15b**. [f] 240 µmol of **15b**. [g] with 420 µmol of **15b** for the threefold ester to anthracene transformation; the third aromatization was induced in a separate step by treatment with concentrated *aqueous* HCl.

[2] Investigations and reactions performed by Christian Fischer

A noteworthy observation in the context of the direct ester to anthracene transformation was done, when an excess of methyl-substituted 1,5-bifunctional organomagnesium reagent **19** (preparation of precursor see chapter 2.7.1) was added to dimethyl phthalate (**20**). Acid **21** was obtained as the single product in 75% yield. This suggests that the alkoxide, formed after the double nucleophilic addition of Grignard reagent **19** reacts with the neighboring ester group forming and intermediary lactone. Subsequent deprotonation of the double benzylic position would induce the aromatization and would open lactone-ring. By this a carboxylate would be formed, which seems to be the privileged reaction pathway in this reaction stetting.



Scheme 49: The direct ester to anthracene transformation with dimethyl phthalate (**20**) as substrate and the suggested reaction mechanism.

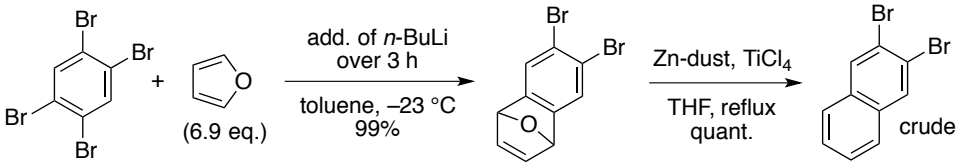
Employing a corresponding organometallic reagent with deuteration in the benzylic position might allow to confirm the reaction mechanism by the detection of deuterium quenched base, in this case the Grignard reagent itself. Intriguingly this reaction is an example, where the aromatization of the direct ester to arene transformation is solely induced by base, respectively with excess of the Grignard reagent and no acidic workup is necessary.

2.3 Direct Transformation of Esters into Tetracenes and Pentacenes

The exceptionally high yields in the direct ester to anthracene transformation suggested to further explore related 1,5-bifunctional organomagnesium reagents. Therefore, the synthesis of elongated polycyclic aromatic systems by the direct ester to arene transformation strategy was investigated. Non-symmetric, 5-substituted tetracenes and particularly interesting, but synthetically challenging mono-substituted pentacene derivatives presented the synthetic goals.

2.3.1 Preparation of Reagent Precursors

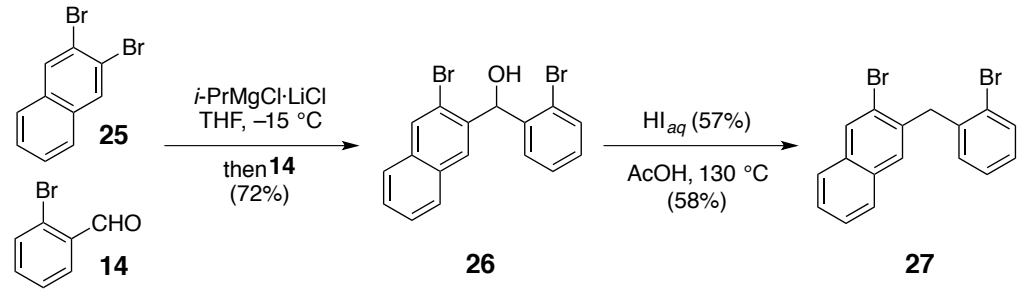
The synthesis of both desired dibromo-reagent-precursors builds upon the strategy described by Piers *et al.*[109] Though the utilized 2,3-dibromonaphthalene (**25**) was prepared according to Hart and coworkers.[112] The in situ benzyne formation *via* 1,2-elimination following the mono-halogen-metal exchange of *tetra*-bromobenzene (**22**) with *n*-BuLi allows the direct Diels-Alder reaction with an excess of furan (**23**). This gave bromo-substituted dihydro-epoxynaphthalene in excellent yield. Following reductive aromatization mediated by low-valent titanium prepared from Zn-dust and $TiCl_4$ delivered the desired 2,3-dibromonaphthalene (**25**) in quantitative yield. **25** was directly used without purification in the subsequent reactions.



Scheme 50: Synthesis of 2,3-dibromonaphthalene (**25**) by a Diels-Alder reaction, followed by a low-valent Titanium mediated reduction.

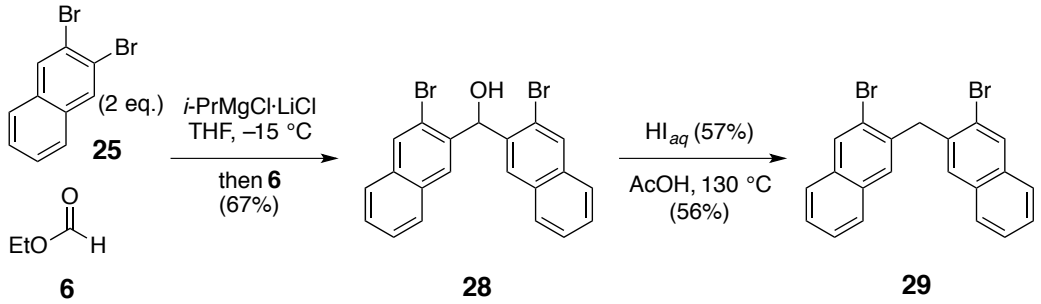
Mono-metalation of **25** with *i*-PrMgCl•LiCl at –15 °C and addition of 2-bromobenzaldehyde (**14**) gave the corresponding diarylmethanol **26** in 72% (Scheme 51). Double benzylic alcohol **26** was dehydroxylated by concentrated hydroiodic acid in acetic acid at high temperature to give the desired dibromo-precursor (**27**). Recrystallization from hot *n*-heptane gave white crystals of **27**,

ready for formation of a 1,5-bifuncitonal organomagnesium reagent to prepare tetracenes.



Scheme 51: Synthesis of reagent-precursor 2-bromo-3-(2-bromobenzyl)naphthalene (**27**).

Following the same strategy, but reacting two equivalents of the mono-metalated intermediate derived from dibromonaphthalene **25** with ethyl formate (**6**) and subsequent dehydroxylation gave access to dibromodiarylmethane **29**, the desired pentacene precursor.



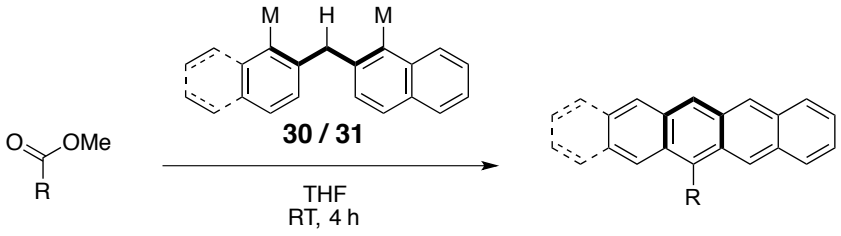
Scheme 52: Synthesis of reagent-precursor bis(3-bromonaphthalen-2-yl)methane (**29**).

2.3.2 Direct Ester to Tetracene and Pentacene Transformation

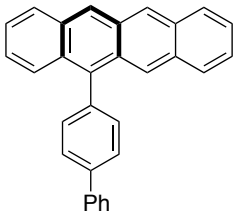
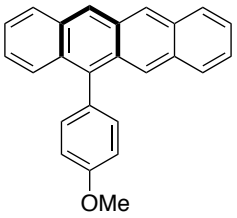
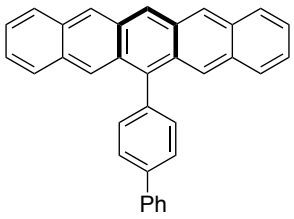
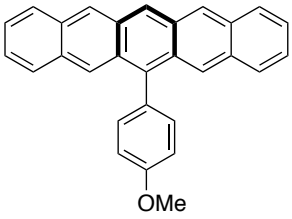
The 1,5-bifunctional organomagnesium reagents **30** and **31** for the direct ester to tetracene, respectively pentacene transformation where prepared and titrated according to the method described for the preparation of Grignard reagent **15b** employed for the anthracene synthesis. The direct magnesiation of the corresponding *o,o'*-dibromodiarylmethanes **27** and **29** with elemental magnesium works smoothly in THF at room temperature. After applying the same conditions like described above for the ester to anthracene transformation (THF, RT, 4 h) and acidic workup, the tetracenes **32a** and **32b** where obtained after purification by column chromatography (Table 7, entry 1 and 2). Mono-substituted pentacenes constitute a very sensitive class of compounds, however

by working in degassed solvents and in the dark, pentacenes **33a** and **33b**, where successfully isolated after evaporation of the ethereal solvents and washing the residue with *n*-hexane under argon (Table 7, entry 3 and 4). The dark-blue colored pentacenes decomposed within 30 min in non-degassed $CDCl_3$ or acetonitrile, however the NMR-samples where stable for at least 12 h in degassed $CDCl_3$ when measured in brown glass tubes.

Table 7: Scope of the direct transformation of esters **3** into tetracenes **32** and pentacenes **33** using the 1,5-bifunctional Grignard reagents **30** respectively **31**.[3]



3 **32 / 33**

Entry[a]	Product[b]	Entry	Product[b]
1	 **32a**, 61%	2	 **32b**, 89%
3	 **33a**, 97%	4	 **33b**, 82%

[a] Reactions performed with 100 µmol ester **3** in THF (1.0 mL) and 140 µmol **30** respectively **31** at RT for 4 h, followed by *aqueous* workup with HCl 1 $molL^{-1}$ [b] Yields of isolated products.

These results demonstrate that the mild reaction conditions of the direct ester to arene transformation allow the synthesis of sensitive compounds like pentacenes in high yields.

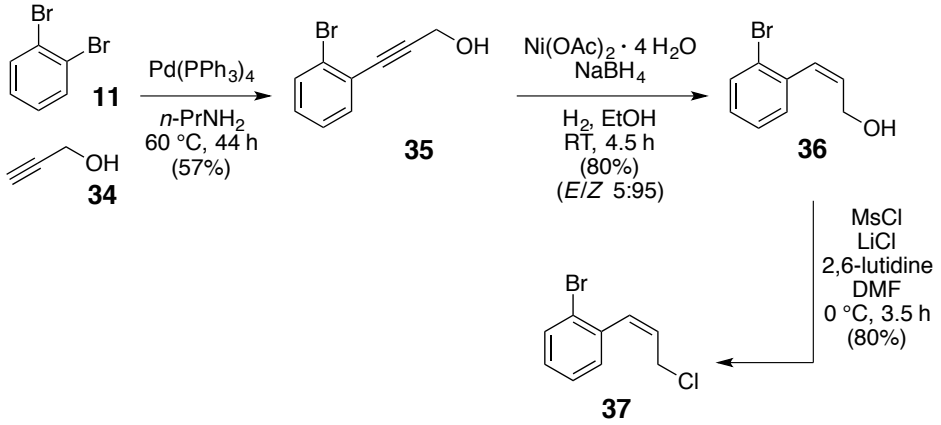
[3] Investigations and reactions performed by Christian Fischer.

2.4 Studies on the Direct Ester to Naphthalene and Phenanthrene Transformation

To further extent the scope of the direct ester to arene transformation the synthesis of naphthalenes and phenanthrenes was explored. The reaction design in this chapter allowed the investigation of a double halogen-metal exchange on an alkyl and aryl-moiety in parallel. A successful reagent preparation would give access to non-symmetric substituted 1,5-bifunctional organomagnesium reagents that might be capable to react with carboxylic acid esters and successively form an arene via an 1,2-elimination.

2.4.1 Preparation of Reagent Precursors

The preparation of the reagent precursor for the naphthalene synthesis started by a one-fold Sonogashira cross-coupling of 1,2-dibromobenzene (**11**) with propargyl alcohol **34**. (*Z*)-selective hydrogenation of the obtained 2-bromophenylpropynol **35** on colloidal nickel gave the corresponding (*Z*)-propenol **36** in 80% yield. Mesylation and in-situ attack of chloride delivered the desired 1,5-dihalogenated precursor **37** in a yield of 80%.

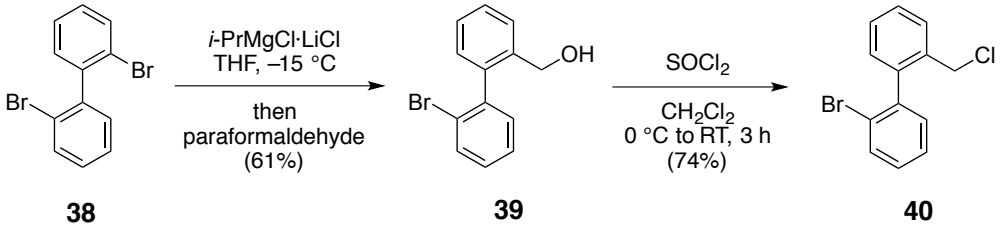


Scheme 53: Synthesis of reagent-precursor (*Z*)-1-bromo-2-(3-chloroprop-1-en-1-yl)benzene (**37**).

The synthesis of the reagent precursor required for the investigation of the direct ester to phenanthrene transformation, commenced by a mono-halogen-metal-exchange of 2,2'-dibromo-1,1'biphenyl[4] (**38**) with *i*-PrMgCl•LiCl followed by the

[4] Prepared and kindly provided by Reto M. Witzig.

addition of paraformaldehyde. Next, the benzylic alcohol **39**, which was obtained in 61% yield, was reacted with thionyl chloride to give the desired 1,5-dihalo-substituted precursor **40** in 70% yield.



38 **39** **40**

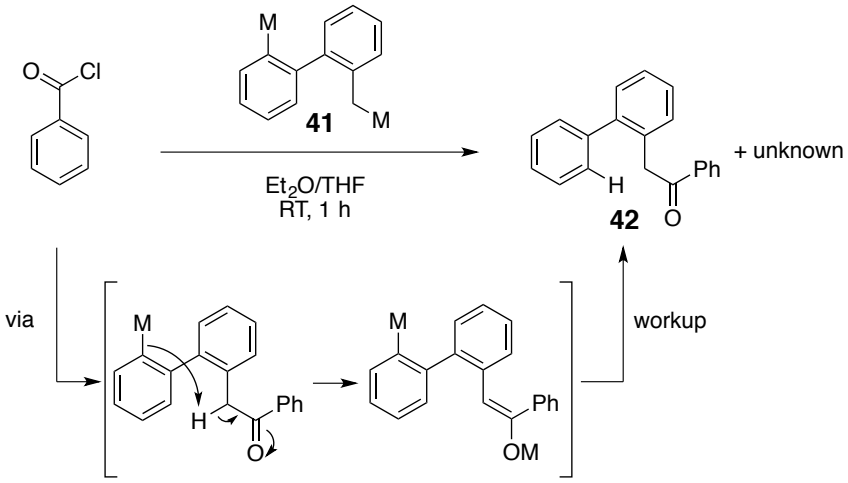
Scheme 54: Synthesis of reagent-precursor 2-bromo-2'-(chloromethyl)-1,1'-biphenyl (**40**).

2.4.2 Studies on the Direct Ester to Naphthalene and Phenanthrene Transformation

Metalation attempts of 1,5-dihalo-precursor **37** with elemental magnesium in Et_2O and THF under several conditions were not successful and did lead to decomposition of the starting material. Analysis by ^{1}H-NMR spectroscopy and GC/MS showed the formation of several products and indicate besides double bond isomerization and allene-formation the formation of diverse dimeric structures. A productive reaction with carboxylic acid ester was not observed.

In contrast, the biphenyl-precursor **40** could be successfully metalated. However, in preliminary magnesiation experiments with the corresponding dibromo-biphenyl derivative, GC/MS analysis suggests the formation of various dimers. Therefore, chloride-derivative **40** was prepared and the magnesiation was first conducted in Et_2O at 0 °C to observe metalation of the benzylic position after 1.5 h. In the following THF was added to facilitate the magnesiation of the aryl bromide. The mixture was stirred for 21 h at RT and GC/MS suggested that about 80% of the desired 1,5-bifunctional organomagnesium reagent **41** were formed. No reaction was observed with methyl anisate, however benzoyl chloride was fully converted to different products. Preparative TLC allowed isolation of a compound contaminated with impurities. NMR-spectroscopy suggested the formation of product **42**. Self-quenching i.e. enolization of an intermediate and subsequent

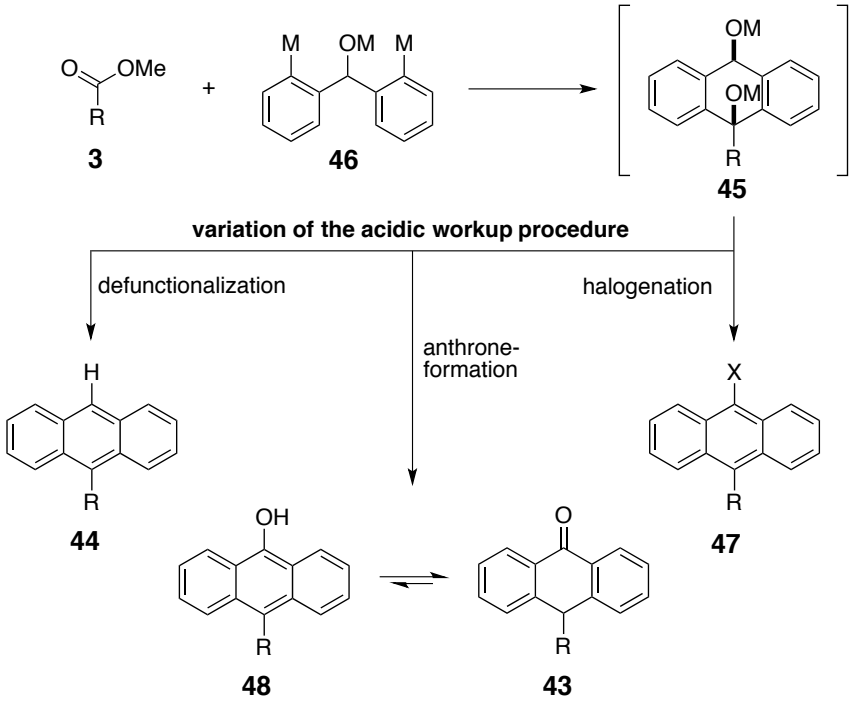
tautomerization during aqueous workup might be an explanation of this reaction outcome (Scheme 55).



Scheme 55: The reaction of 1,5-bifunctional organomagnesium reagent **41** gave small amounts of ketone **42** as main product.

2.5 The Synthesis of Disubstituted Anthracenes by a 1,5-Bifunctional Organomagnesium Alkoxide Reagent

Considering the observation that carboxylic acid esters bearing protic groups were well tolerated in the synthesis of anthracenes raised the question, if it would be feasible to prepare corresponding 1,5-bifunctional organometallic alkoxide reagents. A deprotonation-magnesiation sequence would allow the direct preparation of such a reagent from a 1,5-dibromo-precursor bearing a protic group. The ideal starting material to investigate this approach was bis(2-bromophenyl)methanol (**12**), since a low-cost large scale preparation in a single step from dibromobenzene and 1-bromobenzaldehyde with purification by recrystallization was already established. The double nucleophilic addition of the corresponding 1,5-bifunctional organomagnesium alkoxide reagent **46** would initially lead to the formation of an intermediary bisalkoxide **45**. By variation of the workup conditions the magnesium bisalkoxide would allow the direct further functionalization and give either access to defunctionalized anthracenes **44**, halogenated products **47** or to anthrols **48**, which tautomerize to the corresponding anthrones **43**.

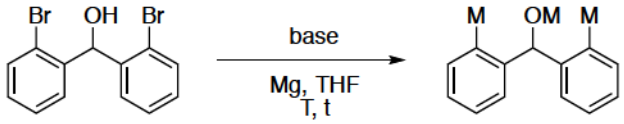


Scheme 56: Outline of the direct ester to disubstituted anthracene and anthrone transformation by reaction of an ester **3** with the alkoxy-functionalized 1,5-bifunctional organomagnesium reagent **46** and variation of the workup conditions.

With the prepared bis(2-bromophenyl)methanol (**12**) in hand, a deprotonation-magnesiation sequence was investigated to prepare the 1,5-bifunctional organomagnesium reagent **46**. Deprotonation of the hydroxy group of **12** was carried out with *n*-Bu_2Mg in THF at RT.[113] The solution of the resulting alkoxide was then added to a suspension of freshly cut magnesium turnings in THF. After heating the reaction mixture repeatedly to mild reflux a change of color of the reaction mixture from colorless to yellow was observed. Based on experience obtained in the course of the prior projects, the color change is an indication for the formation of Grignard reagent. After stirring the reaction mixture for 13 h at RT complete metalation was observed (Table 8, entry 1). However, these conditions turned out to be irreproducible and the desired insertion of the metallic magnesium was only observed occasionally (Table 8, entry 2). Hence, to develop a more reliable protocol for the Grignard reagent preparation, base, solvent and the mixing-order of the reagents was further explored. Deprotonation with *i*-PrMgCl was not successful and switching the base to *i*-PrMgBr and the solvent to 2-Me-THF did also not give the desired 1,5-bifunctional organomagnesium reagent (Table 8, entries 3 and 4). A considerable improvement was observed

when the order of addition of the reagents was inversed. The addition of *i*-PrMgCl to a suspension of freshly cut and under vacuum preheated magnesium turnings in THF, followed by the addition of a solution of bis(2-bromophenyl)methanol (**12**) in THF led immediately to the initiation of the reaction after gently heating to reflux. In all repetitions, the immediate indicative change of color to yellow was observed. After stirring the reaction mixture for 1 h at room temperature the metalation was incomplete (Table 8, entry 5). However, heating the reaction to 60 °C for 1 h efficiently gave the desired 1,5-bifunctional organomagnesium alkoxide reagent **46** (Table 8, entry 6).

Table 8: Development of a deprotonation-magnesiation sequence for the preparation of the 1,5-bifunctional organomagnesium alkoxide reagent **46**.

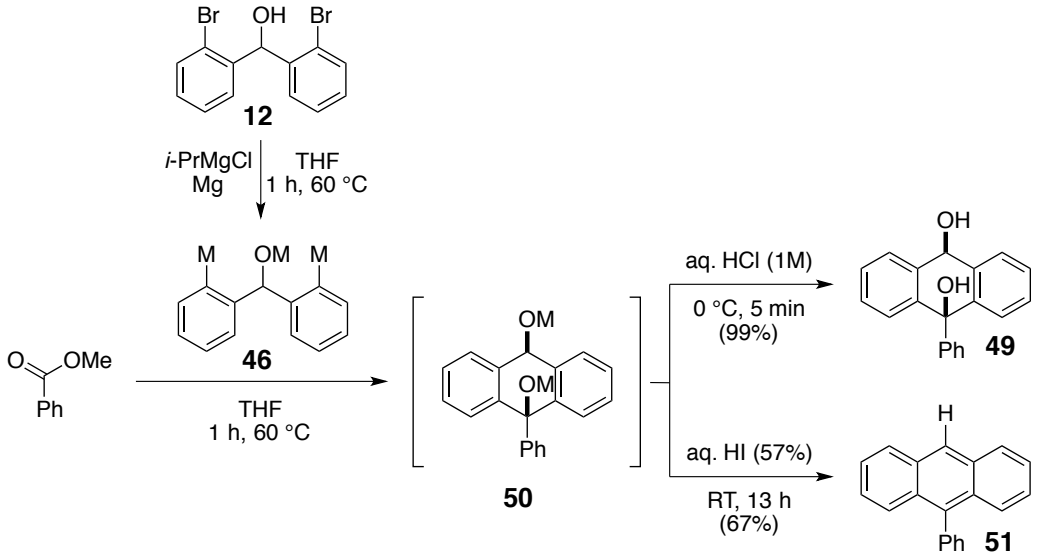


12 **46**

Entry	Base	Addition[a]	T	t	Magnesiation[b]
1	*n*-Bu_2Mg	normal	RT	13 h	✓
2	*n*-Bu_2Mg	normal	RT	13 h	×
3	*i*-PrMgCl	normal	RT	13 h	×
4[c]	*i*-PrMgBr	normal	RT	13 h	×
5	*i*-PrMgCl	inverse	RT	1 h	~
6	*i*-PrMgCl	inverse	60 °C	1 h	✓

[a] Normal: addition of base to a solution of **12** in THF, then addition of the resulting reaction mixture to Mg turnings; inverse: addition of base to Mg, then addition of a solution of **12** in THF to the reaction mixture. [b] ✓ full magnesiation; × no reaction; ~ incomplete magnesiation. [c] reaction in 2-Methyl-THF.

Having established a robust metalation procedure, the reaction of reagent **46** with methyl benzoate as a model substrate was investigated. After treatment of an ester solution in THF with reagent **46** and stirring the mixture at 60 °C for 1 h, full conversion of the ester to the intermediary bisalkoxide **45** was observed. Acidic workup with hydrochloric acid (1 $molL^{-1}$) gave diol **49** as a white crystalline solid in an excellent yield of 99% (Scheme 57).



Scheme 57: Reaction of methyl benzoate with the 1,5-bifunctional organomagnesium alkoxide reagent **46** followed by the specified workup afforded 9-phenyl-9,10-dihydroanthracene-9,10-diol (**49**) and 9-phenylanthracene (**51**).

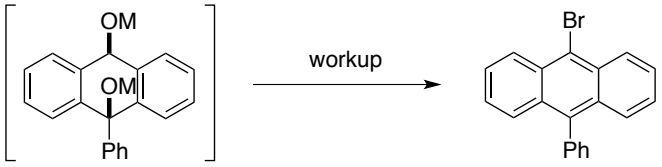
Remarkably, the reaction afforded exclusively the *cis*-diol, which presumably results from coordination of the alkoxide metal of reagent **46** to the ester carboxyl oxygen during the 1,2-addition.

The high efficiency of the double nucleophilic addition of 1,5-bifunctional organomagnesium reagent **46** to methyl benzoate provided the opportunity to study the direct functionalization of magnesium bisalkoxide **50** by variation of the workup conditions. Subsequently, also the chemical modification of the isolated *cis*-diol **49** can be considered as an attractive goal. Direct workup with concentrated aqueous hydroiodic acid (57%) for 13 h at room temperature led to reductive defunctionalization and yielded 67% of 9-phenylanthracene (**51**) under these non-optimized conditions (Scheme 57).

Next, conditions for the direct synthesis of 9-bromo-10-phenylanthracene (**52**, Table 9) were investigated. To prevent bromide/chloride scrambling, the Grignard reagent **46** was prepared after deprotonation of bis(2-bromophenyl)methanol (**12**) with *n*-Bu_2Mg or *i*-PrMgBr *via* the developed inverse-addition magnesiation protocol. Addition of concentrated aqueous hydrobromic acid to a solution of intermediate **50** delivered the desired brominated product **52**, after stirring the mixture for 1 h at room temperature,

accompanied with undesired defunctionalized compound **51** (Table 9, entry 1) in a 2:3 ratio. Employing NaBr in excess to increase the bromide ion concentration prior to the acidic workup did not improve the product ratio to a significant extent (Table 9, entry 2). When using aqueous HBF_4 the bromide ions originating from precursor **12** were capable to give the desired product **52**, however the amount of defunctionalized product **51** increased leading to a ratio of 3:7 (Table 9, entry 3). Deprotonation of reagent precursor **12** with *i*-PrMgBr and workup with pure triflic acid allowed to isolate 45% of the desired brominated anthracene, but purification was laborious since THF polymerized under these conditions (Table 9, entry 4). To improve product distribution, residual magnesium was removed by cannulation of the reaction solution into a separate flask. Introduction of anhydrous gaseous HBr, prepared by thermolysis of triphenylphosphonium bromide in refluxing xylene,[114] into the reaction solution at room temperature gave brominated product **52** in 52% yield (Table 9, entry 5). Finally, successive addition of glacial acetic acid and BF_3•OEt_2 delivered the desired 9-bromo-10-phenylanthracene (**52**) in a yield of 65% yield (Table 9, entry 6).

Table 9: Optimization of the workup conditions for the synthesis of 9-bromo-10-phenylanthracene (**52**).

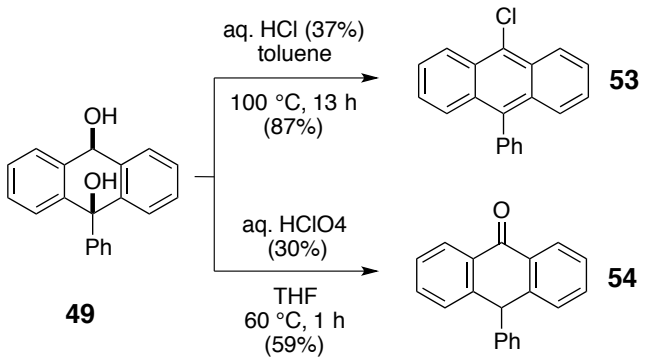


50 **52**

Entry	Base[a]	Acidic workup	T	t	Ratio **52**/**51** or yields[b]
1	*n*-Bu_2Mg	aq. HBr (48%)	RT	60 min	40:60
2	*n*-Bu_2Mg	aq. HBr (48%), NaBr (7 eq.)	RT	15 min	42:58[c]
3	*n*-Bu_2Mg	HBF_4 (50%)	RT	60 min	29:71
4	*i*-PrMgBr	TfOH	RT	30 min	45% (**52**) 21% (**51**)
5[d]	*i*-PrMgBr	anhydrous HBr (g)	RT	30 min	52% (**52**) 19% (**51**)
6[d]	*i*-PrMgBr	AcOH, BF_3•OEt_2	60 °C	60 min	65% (**52**)

[a] Base employed for the deprotonation of **12** following the inverse-addition protocol [b] Entries 1–3: ratios of **52**/**51** determined by ^{1}H-NMR (**52**: δ = 8.61; **51**: δ = 8.49); entries 4–6: isolated yields after column chromatography on silica gel [c] formation of anthrone observed. [d] the reaction mixture was separated from residual magnesium by cannulation into a separate flask before introducing dry gaseous HBr.

Next, we aimed to prepare the corresponding 9-chloro-10-phenylanthracene (**53**) directly from intermediate magnesium bisalkoxide **50** by a workup method. For this, the reagent precursor **12** was deprotonated with *i*-PrMgCl prior to magnesiation and in the workup step a solution of dry HCl (4 molL^{-1}) in dioxane was added in an attempt to precipitate competing bromide as $MgBr_2$. Nonetheless, a mixture of 9-bromo (**52**) and 9-chloro-10-phenylanthracene (**53**) was obtained, which could not be separated by column chromatography nor by other methods. With a highly efficient reaction to diol **49** already established, a two-step procedure was considered next. Therefore, a solution of isolated diol **49** in toluene was treated with hydrochloric acid (37%) at 100 °C for 13 h, which gave the desired chlorinated product **53** in a respectable yield of 87% (Scheme 58). Furthermore, the synthesis of anthrol was envisioned, which tautomerizes to 10-phenylanthracen-9(10*H*)-one (**54**) under the acidic workup conditions. First, a solution of diol **49** in THF was treated with aqueous H_2SO_4, which gave the desired product in an inseparable mixture with unknown decomposition products. In contrast, stirring a solution of diol in THF with aqueous $HClO_4$ (30%) for 1 h at 60 °C, allowed to isolate anthrone **54** in 59% yield.



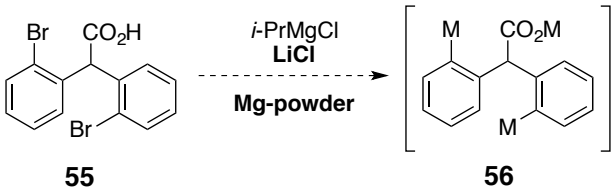
Scheme 58: Synthesis of 9-chloro-10-phenylanthracene (**53**) and 10-phenylanthracen-9(10*H*)-one (**54**) from diol **49** under acidic conditions.

Magnesiation of 2,2-Bis(2-bromophenyl)acetic acid

Interesting to note in this context is the observation that the developed deprotonation-magnesiation protocol developed, did not allow to prepare a reactive 1,5-bifunctional organomagnesium reagent from 2,2-bis(2-bromophenyl)acetic acid[5] (**55**) (Scheme 59). Partial dehalogenation, presumably

[5] Prepared and kindly provided by Christian Fischer.

magnesiation, at room temperature was only observed after sonification and elongated reaction times (18 h: approx. 31%, 48 h: approx. 56%) or at elevated temperatures (75 °C, 2.5 h: 82%), but a productive reaction with a carboxylic acid ester was never observed.

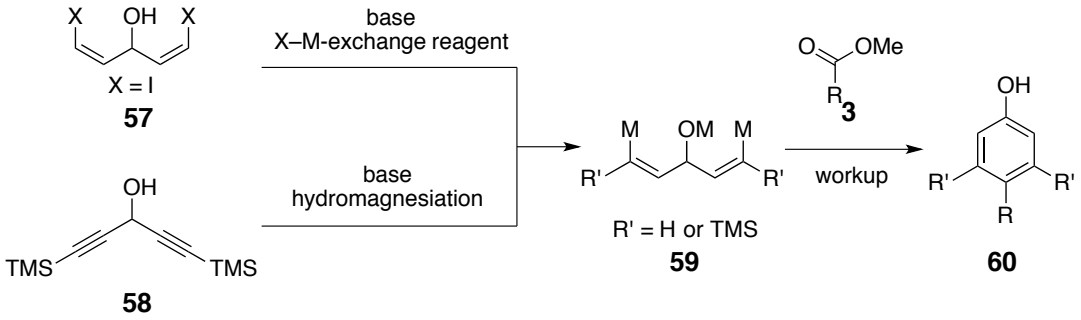


Scheme 59: Acceleration of the magnesiation of substrate **55** by LiCl addition and use of Mg-powder might allow to access to the corresponding bifunctional organomagnesium reagent **56** in future.

Based on experience made after these experiments (see chapter 2.8.4) an attempt to accelerate the magnesiation by the addition of LiCl and by using Mg-powder, instead of Mg-pieces, appears to be a very promising strategy for the successful preparation of an active reagent **56** in future.

2.6 The Direct Ester to Phenol Synthesis

After having developed the direct ester to benzene transformation and the deprotonation-magnesiation protocol in the previous chapter the related direct ester to phenol transformation was investigated. The required 1,5-bifunctional organomagnesium alkoxide reagent **59** was envisaged to be either accessible by a halogen-metal exchange reaction starting from the already synthesized precursor **57** or alternatively by a direct double hydromagnesiation of ready available bisalkyne **58**.

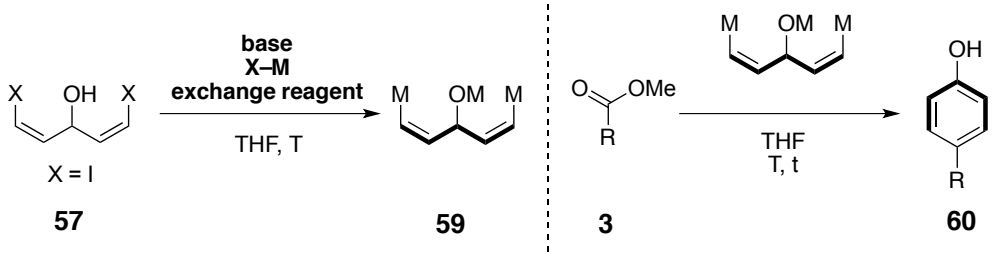


Scheme 60: Strategies to prepare a 1,5-bifunctional organometallic alkoxy reagent **59** to develop a direct ester to phenol transformation.

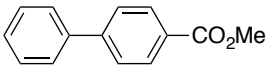
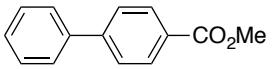
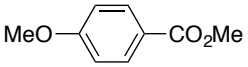
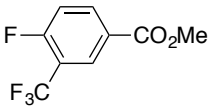
Halogen-metal-exchange

The screening to access a 1,5-bifunctional organometallic species **59** commenced by the addition of *n*-Bu_2Mg to a solution of (1*Z*,4*Z*)-1,5-diiodopenta-1,4-dien-3-ol (**57**) in THF at –20 °C. After a short time, the formation of a white suspension indicated successful deprotonation and the halogen-metal exchange reagent *i*Pr*n*Bu_2MgLi was added. Immediately, a clear solution was formed and after 15 min methyl 4-phenylbenzoate (**3a**) was added. Then the reaction mixture was stirred for 2 h. The ^{1}H-NMR spectra of the crude reaction mixture suggested that the ester was partially attacked by butyl-groups and was furthermore accompanied with partial decomposition of dihaloprecursor **57**. In the following the X–M-exchange reagent was switched to *n*-BuLi. GC/MS analysis of a reaction aliquot proved the completeness of the halogen-metal exchange after 15 min at –20 °C. However, after ester addition, no desired product could be isolated and most of the ester did not convert. Broad peaks in the ^{1}H-NMR spectra indicated decomposition and the low stability of the formed bifunctional organometallic reagent. Therefore, the reaction temperature was lowered to –78 °C and after addition of ester **3a** the reaction mixture was allowed to warm to RT over 4 h. However, the insolubility of the products prevented isolation of the potentially formed desired phenol. Thus, next methyl anisate **3j** was employed as electrophile under the same conditions. This allowed to obtain about 12% of the desired phenol, contaminated with some impurities. A final experiment with the electron-poor fluorinated ester **3b** and analysis of the crude reaction mixture by ^{19}F-NMR revealed the formation of various unknown side products and confirmed a low efficiency of the reaction under these conditions.

Table 10: In situ generation of the reagent 1,5-bifunctional organomagnesium alkoxide reagent **59**[a] and optimization of the reaction parameters of the direct ester to phenol transformation.

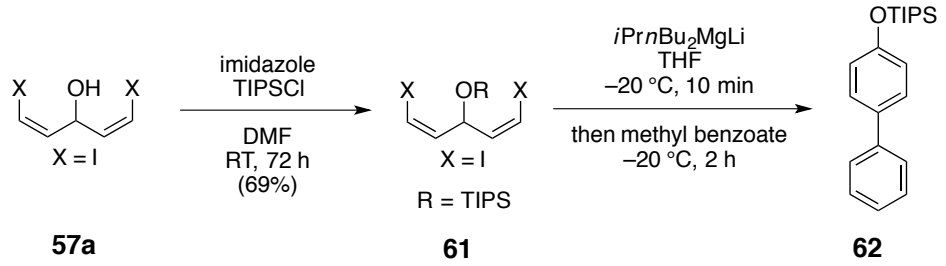


57 **59** **3** **60**

Entry	X-M-exchange reagent[b]	Ester[c]	T	t	yield[d]
1	*i*Pr*n*Bu$_2$MgLi[e]		–20 °C	2 h	—
2	*n*-BuLi		–20 °C	2 h	—
3	*n*-BuLi		–78 °C	4 h	—
4	*n*-BuLi		–78 °C	4 h	12%
5	*n*-BuLi		–78 °C	4 h	—

[a] Deprotonation of (1*Z*,4*Z*)-1,5-diiodopenta-1,4-dien-3-ol (**57**) (2.00 eq.) with equimolar amounts of *n*-Bu$_2$Mg in THF at T for 5 min. [b] Reaction with X-M exchange reagent (4.00 eq.) at T for 15 min. [c] Addition of ester **3** (1.00 eq) and reaction at T for t followed by aqueous work-up (HCl 1.0 molL^{-1}). [d] Yield of isolated product. [e] Freshly prepared from *i*-PrMgCl (1.00 eq)and *n*-BuLi (2.00 eq).

Based on the results of the preceding experiments it was decided to protect the hydroxy-group of diiodo-precursor **57** prior to the halogen-metal exchange reaction. First, the corresponding triisopropylsilylether derivative **61** (TIPS group) was prepared.[115] Though, this derivative could not be completely purified by column chromatography, the double halogen-metal exchange with magnesiate *i*-Pr*n*-Bu$_2$MgLi and following reaction with methyl benzoate allowed to isolate 14% of the desired protected phenol **62**.

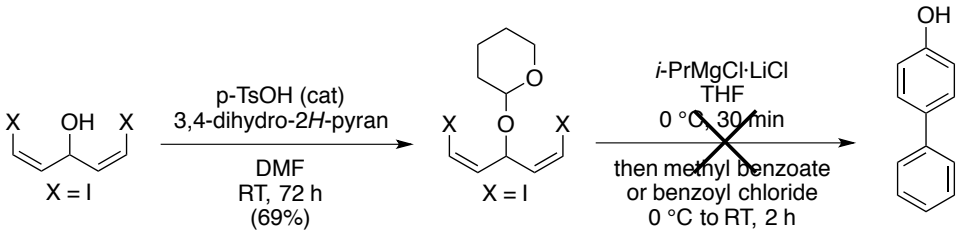


57a **61** **62**

Scheme 61: TIPS protection of (1*Z*,4*Z*)-1,5-diiodopenta-1,4-dien-3-ol (**57**) and following halogen-metal-exchange with *i*Pr*n*Bu$_2$MgLi allowed to prepare TIPS-protected phenol derivate **62** in 14% yield.

Speculating, that the bulky TIPS-group might hamper the double nucleophilic addition of the 1,5-bifunctional organometallic reagent protic precursor **1a** was tried to be converted to the corresponding methyl-ether.[116] However, deprotonation with sodium hydride and quenching with methyl iodide in THF at RT led to complete decomposition of the starting material.

With the intention to facilitate the halogen-metal exchange and to stabilize a potentially accessible organometallic reagent by a second coordinating oxygen-atom, alcohol **1a** was successfully protected with a tetrahydropyranyl-group (THP).[117] Though, GC/MS-analysis suggested partial two-fold halogen-metal exchange of precursor **63** with *i*-PrMgCl•LiCl in THF after 30 min at 0 °C, no subsequent reaction could be observed with neither methyl benzoate nor with more reactive benzoyl chloride.

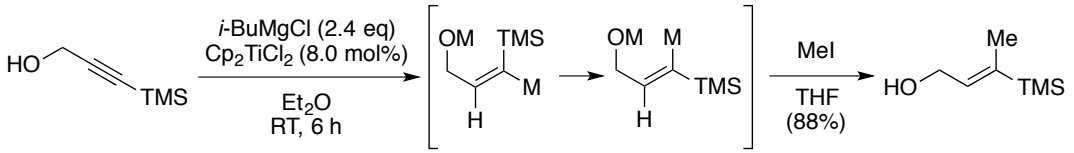


1a **63**

Scheme 62: THP-protection of (1*Z*,4*Z*)-1,5-diiodopenta-1,4-diene (**1a**) presumably allowed partial metalation with *i*-PrMgCl•LiCl, however no reaction with methyl benzoate or benzoyl chloride was observed.

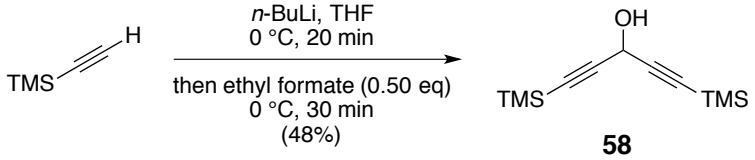
Hydromagnesiation Studies

In an afford to shorten the substrate preparation i.e. to avoid the halogenation and reduction steps and the necessity to perform a halogen-metal exchange reaction, the direct two-fold hydromagnesiation of bis-alkyne **58** to access the corresponding 1,5-bifunctional organomagnesium alkoxide reagent **59** was investigated. This study is based on the literature-known hydromagnesiation of disubstituted alkynes. Intriguingly, Sato reported that TMS-substituted propargylic alcohols readily undergo hydromagnesiations with alkyl Grignard reagents (i.e. *iso*-butylmagnesium chloride) in the presence of catalytic amounts of Cp_2TiCl_2.[118] The proposed mechanism proceeds via a highly regioselective *syn*-addition of intermediary formed Cp_2TiH across the triple-bond, which is followed by transmetalation to give the desired alkenylmagnesium halides under regeneration of the catalytically active titanium hydride species.[119] TMS-substituted propargylic alcohols isomerize to the more stable *trans* alkenyl-organometallic compounds. With this efficient method, alkenyl Grignard reagents are directly accessible from alkynes, which can serve as versatile nucleophiles for the preparation of various (*E*)-3-trimethylsilylalk-2-en-1-ols.



Scheme 63: Sato's titanium-hydride catalyzed hydromagnesiation of 3-(trimethylsilyl)prop-2-yn-1-ol to give (*E*)-3-(trimethylsilyl)but-2-en-1-ol in high yield.

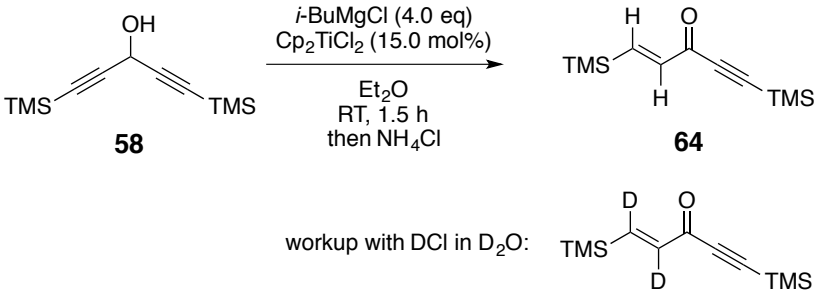
Our investigations commenced with the straightforward preparation of the starting material. The required TMS-substituted bisalkyne **58** was obtained after the two-fold addition of lithium (trimethylsilyl)acetylide to ethyl formate in THF in 48% yield under non-optimized conditions (Scheme 64).[120]



Scheme 64: Synthesis of TMS-substituted bisalkyne **58** by the double addition of lithium (trimethylsilyl)acetylide to ethyl formate.

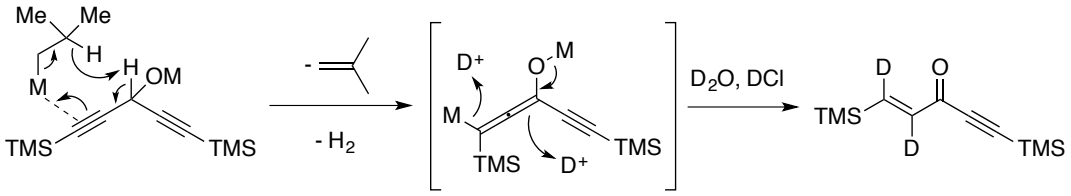
Substrate **58** was treated with *i*-BuMgCl (4.0 eq.) and Cp_2TiCl_2 (15 mol%) under conditions as described by Sato (Scheme 65). Interestingly, the major product

obtained was identified as ketone **64**. The same observation was made under several different conditions as for example with THF as solvent, *i*-PrMgCl as a base, at higher temperature and with $NiCl_2$ as catalyst. Intriguingly, quenching the reaction with D_2O led to two-fold deuterium incorporation across one triple bond.



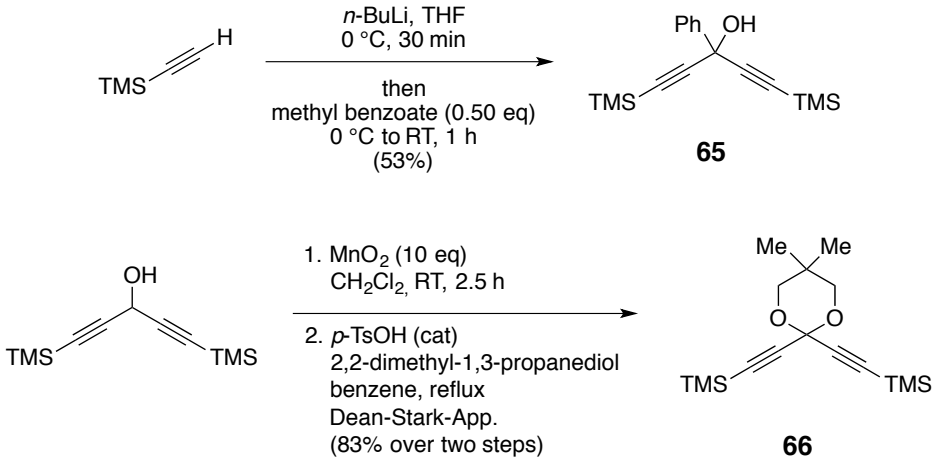
Scheme 65: Substrate **58** was mainly converted to ketone **64** under Sato's hydromagnesiation conditions.

Based on this observations we recognized, that the main difference between the mono-alkynylated propargylic alcohol investigated by Sato and bisalkyne **58** is the acidity in the 3-position. The following mechanistic consideration might be an explanation for the reaction outcome.



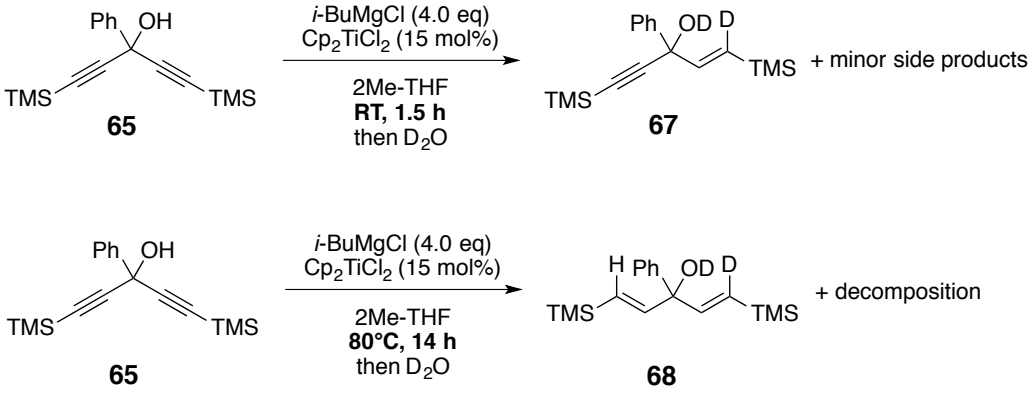
Scheme 66: Proposed reaction mechanism for the formation of ketone **64** in deuterated form.

It was therefore concluded that the acidic bisalkynylated C–H-function prevented the successful hydromagnesiation of starting material **58**. Therefore, two substrate-derivatives were synthesized that do not bear this acidic proton. Phenyl derivative **65** was prepared in 53% yield by double alkynylation of methyl benzoate, while acetal **66** was obtained in 83% overall yield after oxidation of **58** with MnO_2 followed by the *p*-TsOH catalyzed acetalisation of the resulting ketone with 2,2-dimethyl-1,3-propanediol (Scheme 67).



Scheme 67: Synthesis of bisalkyne derivatives that do not bear an acidic functionality.

The following partial mono-hydromagnesiation of substrate **65** could be achieved under Sato's conditions in Et_2O by an elongated reaction time of 44 h. While in THF, the hydrometalation was even slower and only traces of the mono-reduced product were detected after aqueous workup, the reaction in 2-MeTHF was faster. However, reduction of both triple-bonds was only achieved after stirring the reaction at 80 °C for 14 h. Quenching a reaction aliquot with D_2O, however indicated no successful metalation, since only monodeuterated compound **68** could be observed in the crude ^{1}H-NMR spectrum accompanied with decomposition products. Addition of methyl benzoate further revealed that no reaction occurred with an ester.

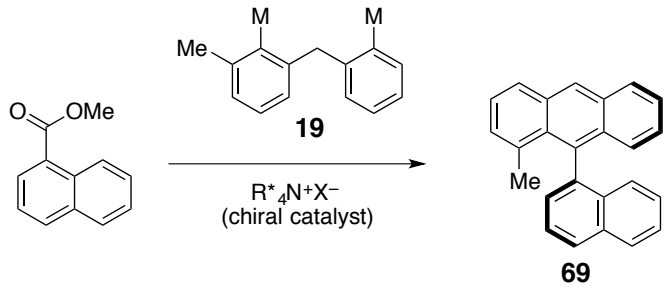


Scheme 68: Fast hydromagnesiation was detected in 2-MeTHF. However, the two-fold hydromagnesiation could not be achieved.

Attempts to hydromagnesiate compound **66** were not successful and only starting material and decomposition products were observed under various conditions.

2.7 Studies on the Stereoselective Transformation of Esters into Substituted Chiral Anthracenes

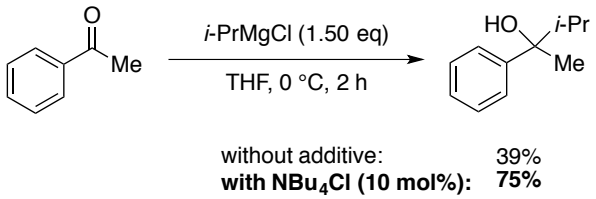
After the successful development of the direct ester to arene transformation, a prime objective of the research project became the realization of a stereoselective reaction in the context of this methodology. The observation that catalytic amounts of quaternary ammonium salts are capable to activate the applied 1,5-bifunctional organomagnesium reagents (see chapter 2.2.2) evoked the question, if chiral ammonium salts would be able to catalytically induce stereoselectivity in a related reaction setting. To explore this idea, the reaction of an non-symmetrically substituted 1,5-bifunctional organometallic reagent with a non-symmetric and sufficiently substituted ester was envisioned to form axially chiral products (Scheme 69). To ensure a comparable reactivity and stability of the non-symmetric reagent, it was convenient to prepare a scaffold similar to the reagent-structure employed in the direct ester to anthracene transformation. A methyl-group in *ortho*-position to one nucleophilic center was introduced into the biphenylmethane-system. By changing the substitution next to one reactive center the symmetry of the former reagent was broken and an unsymmetric substituted 1,5-bifunctional organometallic reagent **19** became available (preparation of reagent-precursor see chapter 2.7.1).



Scheme 69: Reaction design to investigate the stereoselective direct ester to anthracene transformation catalyzed by a chiral catalyst.

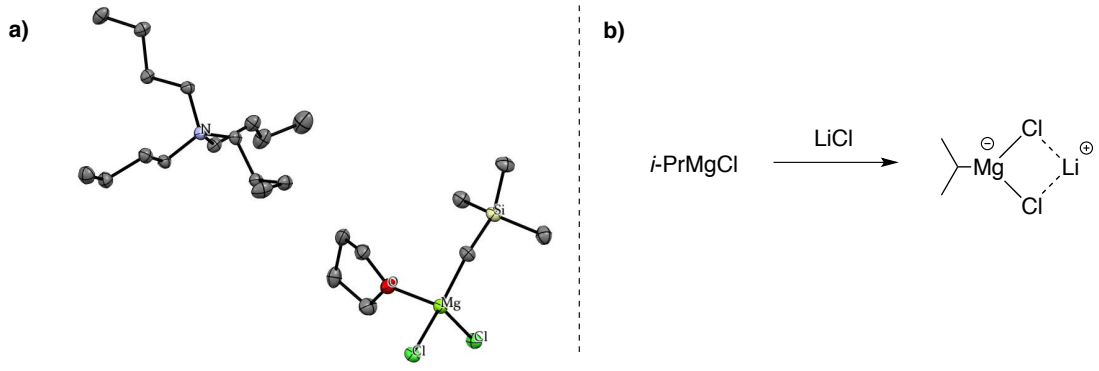
Relevant to the observations in this project, the beneficial effect of quaternary ammonium salts on nucleophilic additions of Grignard reagents to carbonyl compounds have been previously reported.[121] Song showed, that even catalytic amounts of NBu_4Cl are sufficient to significantly minimize the formation of reduction and enolization side products.[122] This observation was proposed to

result from a shift of the Schlenk equilibrium, respectively of the formation of a dinuclear Grignard-reagent-salt complex ($R_2Mg{\bullet}MgX_2$), which favors the addition reaction pathway.



Scheme 70: The beneficial salt effect of catalytic amounts quaternary ammonium salt NBu_4Cl in the addition of Grignard reagents to acetophenone reported by Song.

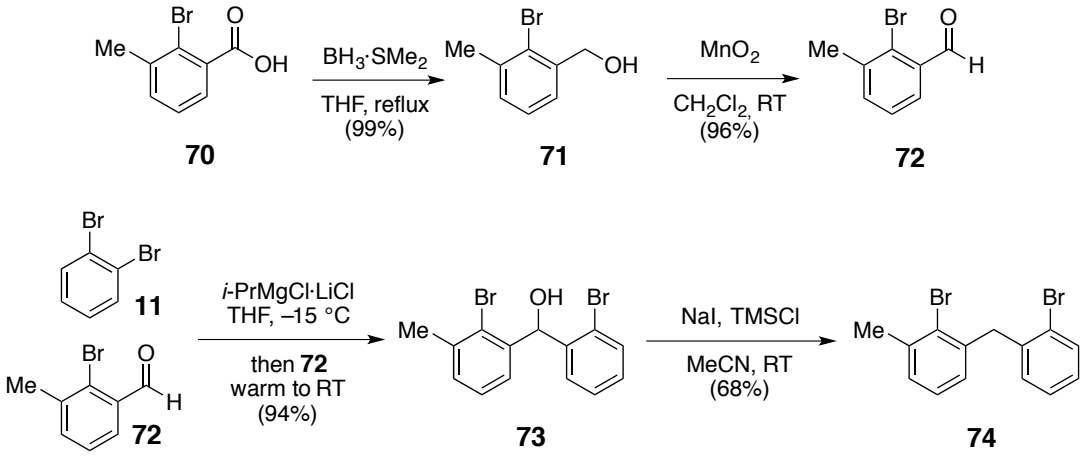
Intriguingly, Hevia and coworkers observed the formation of a monomeric magnesiate, while investigating Grignard reactions in protic deep eutectic solvents.[123] Mixing the Grignard reagent Me_3SiCH_2MgCl with NBu_4Cl in THF afforded 87% of crystals of the magnesiate $[\{NBu_4\}^+\{(THF)Cl_2Mg(CH_2SiMe_3)\}^-]$, which was fully characterized by X-ray crystallography. NMR-studies confirmed that the magnesiate structure is retained in solution. These results suggest, that the beneficial effect of quaternary ammonium salts may be best attributed to the fact that anionic species (magnesiates) are formed, which show an enhanced nucleophilicity compared to neutral organomagnesium reagents. This explanation is in accordance with Knochel's interpretation, that attributes the higher reactivity and nucleophilicity of the "Turbo-Grignard" reagent (*i*-PrMgCl•LiCl) to its magnesiate character.[27]



Scheme 71: a) The X-ray crystal structure of Hevia's magnesiate $[\{NBu_4\}^+\{(THF)Cl_2Mg(CH_2SiMe_3)\}^-]$. H-atoms are omitted for clarity (CCDC 978224). b) Illustration of the partial magnesiate character of Knochel's Turbo-Grignard.

2.7.1 Preparation of Unsymmetric Reagent-Precursor 2-Bromo-1-(2-bromobenzyl)-3-methylbenzene

The preparation of the methyl-substituted unsymmetric *o*,*o*'-dibromodiarylmethane **74** commenced by the reduction of commercially available 2-bromo-3-methylbenzoic acid (**70**). Initial experiments showed that direct reduction of the carboxylic acid to the corresponding aldehyde with DIBAL[124] at low temperature or with pyrrolidine-Red-Al®-system[125] at RT is not efficient, since product formation is accompanied with over-reduction, leading to a mixture of starting material, aldehyde and alcohol. Therefore, complete reduction with BH_3•SMe_2 in refluxing THF to the alcohol **71**, followed by oxidation with MnO_2 in CH_2Cl_2 at RT turned out to be the superior approach and delivered methyl-substituted aldehyde **72** in an overall yield of 95%.

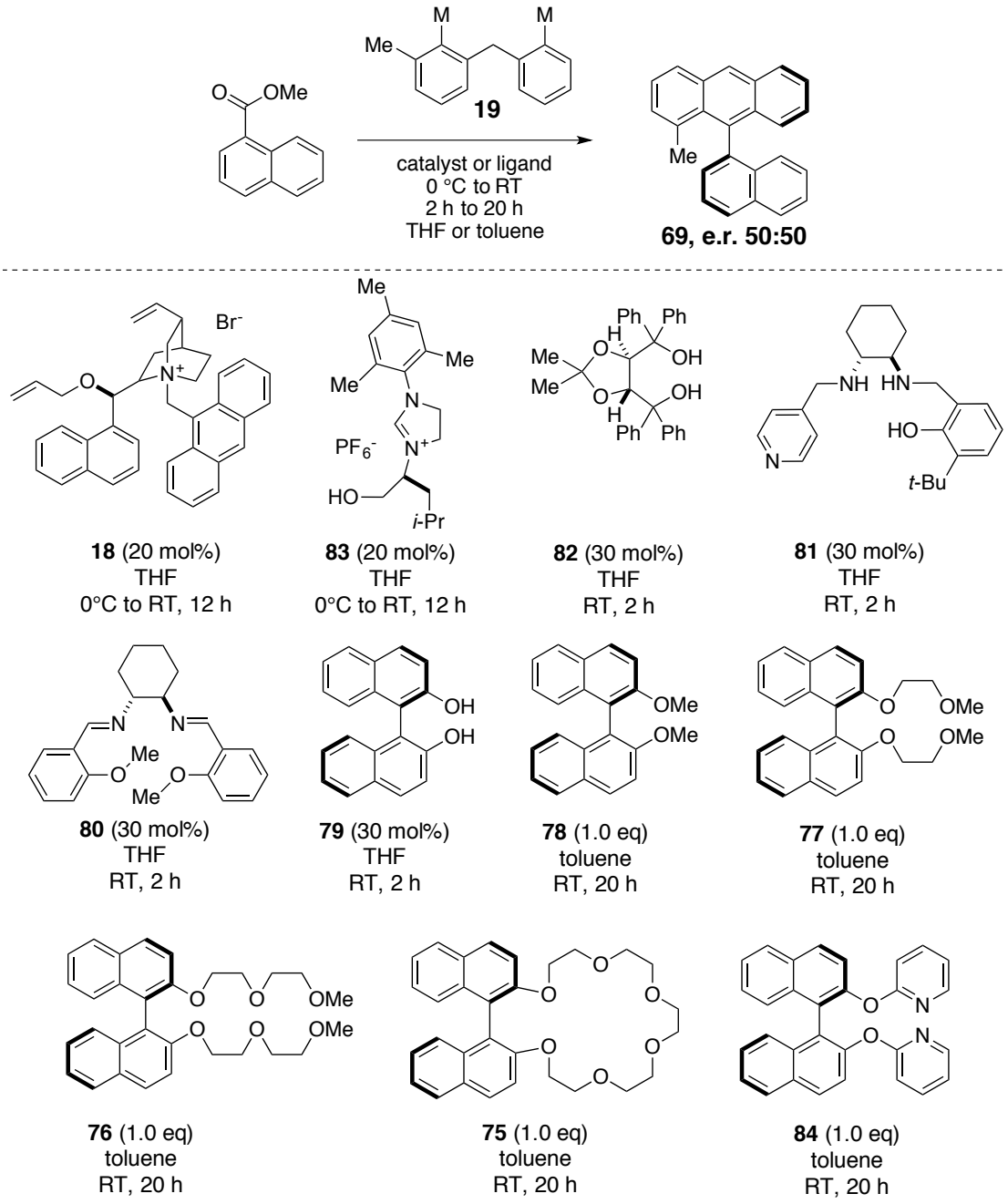


Scheme 72: Synthesis of methyl-substituted unsymmetric o,o'-dibromoarylmethane **74** starting from 2-bromo-3-methylbenzoic acid (**70**).

Mono-halogen-metal exchange of 1,2-dibromobenzene (**11**) with *i*-PrMgCl•LiCl and addition of aldehyde **72** gave the corresponding methyl-substituted diarylmethanol **73** in an excellent yield of 94%. The following TMS-iodide mediated dehydroxylation gave the desired methyl-substituted dibromo-precursor **74** under non-optimized conditions in a yield of 68%.

2.7.2 Studies on a Stereoselective Ester to Anthracene Transformation by the Addition of Chiral Salts and Ligands

Dibromo-precursor **74** was magnesiated with elemental magnesium as described for the corresponding reagent **15b** employed for the anthracene synthesis (see chapter 2.2.2) giving the desired unsymmetrical 1,5-bifunctional organomagnesium reagent **19**. Methyl 1-naphthoate was chosen as model substrate.

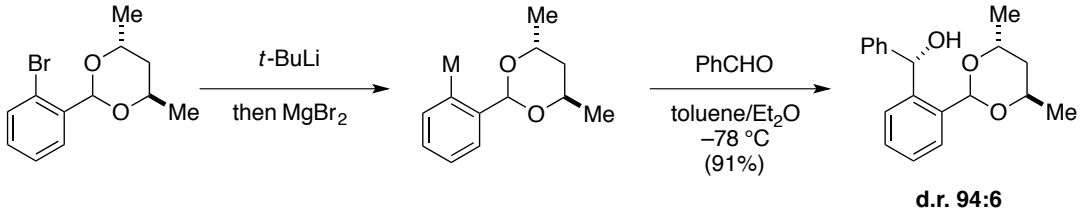


Scheme 73: Screening of diverse catalysts and ligands for a stereoselective direct ester to substituted anthracene transformation.

With this reaction setting, the influence of the chiral catalysts and ligands on the stereoselectivity of the direct ester to substituted anthracene transformation was investigated (Scheme 73). For the reactions in toluene, reagent preparation in THF was followed by solvent evaporation in high vacuum (3 x 10^{-2} mbar) for 45 min at RT. Then toluene and the chiral ethers where added, followed by ester addition. In all reactions under the conditions specified in Scheme 73 product formation could be observed, however no stereoindunction and only racemic product **69** was isolated.

2.8 The Direct Stereoselective Transformation of Esters into Axially Chiral TMS-Naphthalenes

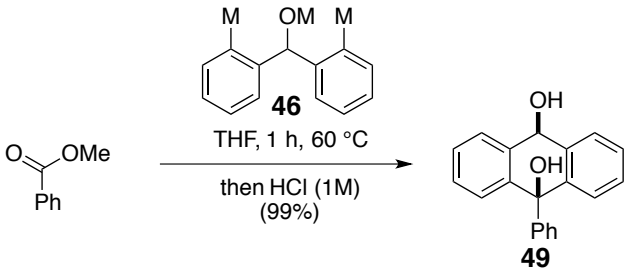
The nucleophilic centers of aryl- and alkenyl-organometallic reagents are achiral, since they are sp^2-hybridized. A well-known strategy to perform stereoselective reactions with such reagents is to introduce chiral heteroatom containing groups next to the anionic centers, which are coordinating to the metals bound to these centers[126] Consequently, the metal becomes stereogenic and can coordinate, respectively attack an electrophile (e.g. carbonyl) stereoselectively. For example, Yamamoto prepared chiral organometallic reagents from 2-bromobenzaldehyde by acetylation with a chiral diol, followed by a halogen-metal exchange with *t*-BuLi.[127] Transmetalation from the corresponding Li-organyl to the Grignard reagent improved the diastereoselectivity from 60:40 to 94:6.



Scheme 74: Yamamoto's chiral Grignard reagents react with aldehydes at low temperatures with good stereoselectivities.

The coordination of metal-alkoxides, created by the deprotonation of alcohols with Grignard bases (e.g. with *i*-PrMgCl like described in Chapter 2.5) have not been described in detail. Especially intriguing was the observation that the coordination of the alkoxide group of organometallic reagent **46** to the carboxyl

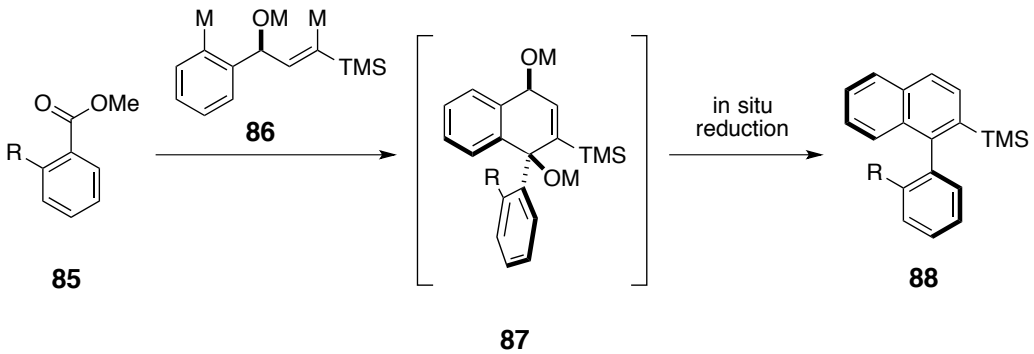
oxygen of an ester leads, even at a temperature of 60 °C, exclusively to the formation of the *cis* stereoisomer **49** in an excellent yield of 99% (Scheme 75).



Scheme 75: Exclusive formation of one *cis*-stereoisomer of diol **49**.

This indicates the presence of a strong and tight intramolecular coordination during the stereo-determining step, which enables, a fully stereospecific reaction at such high, non-cryogenic temperatures.

Recognizing this, the direct ester to arene transformation provides the ideal platform to investigate the employment of an enantiomerically pure organometallic alkoxide reagent and to provide the opportunity to synthesize valuable enantioenriched products from readily available starting materials. We envisioned that the reaction of a chiral 1,5-bifunctional organomagnesium alkoxide reagent **86** with sufficiently substituted carboxylic acid esters **85** would exclusively give the corresponding chiral bisalkoxides **87**. By developing an applicable in situ reduction of intermediate **87**, the stereochemical information of the reagent would be introduced into the axially chiral products **88** via a central to axial chirality conversion in a one-pot reaction setting.



Scheme 76: Stereoselective double nucleophilic addition of a chiral 1,5-bifunctional organomagnesium alkoxide reagent **86** to *ortho*-substituted carboxylic acid esters **85** followed by in situ reduction to give axially chiral naphthalenes **88**.

By this the alkoxy-group would serve as a traceless chiral auxiliary. The TMS-group is considered to allow the direct preparation of organometallic reagent **86** from the corresponding TMS-protected chiral propargylic alcohol by hydrometalation and presumably will stabilize the resulting organometallic reagent. In the further course of the reaction the sterically demanding silane-group increases the rotational barrier of bisalkoxide **87** ideally preventing intermediary racemization. Additionally, it enables to develop a novel synthetic access to arylsilanes by de novo construction of an aromatic ring. Arylsilanes are versatile carbanion surrogates, which can be cross-coupled or functionalized by various methods. The ideal reactivity of carboxylic acid esters in the direct ester to arene transformation is considered to allow the development of a high yielding atroposelective reaction at mild, but non-cryogenic temperatures. Combined with the prospective to straightforwardly prepare diverse chiral 1,5-bifunctional reagents and combine them with ubiquitous esters, the method promised to constitute a highly modular and powerful approach to synthesize unsymmetric substituted axially chiral products.

Chiral propargylic alcohols are readily available starting materials which can be synthesized by direct stereoselective alkynylations,[128] by enzymatic[129] or non-enzymatic[130] (dynamic) kinetic resolutions or by stereoselective reductions of the corresponding ynones.[131] Therefore, they represent ideal starting materials to develop a scalable and flexible synthesis of chiral 1,5-bifunctional organometallic reagent **86** or corresponding derivatives starting from various 2-bromo-benzaldehydes.

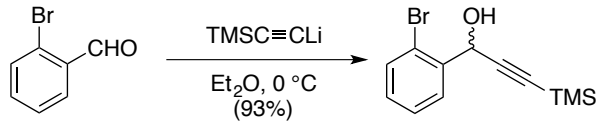
2.8.1 Hydrometalation Studies to Directly Prepare an Organometallic Alkoxide Reagent for the Direct Ester to Naphthalene Synthesis

Hydromagnesiation

At the outset of the project, a deprotonation-hydromagnesiation-magnesiation sequence of a suitable propargylic alcohol was envisioned to access directly a 1,5-bifunctional organomagnesium reagent **86** capable for a direct ester to naphthalene transformation. This hydromagnesiation approach builds upon the

known successful hydromagnesiation of chiral enantioenriched TMS-substituted propargylic alcohols reported by Sato (see also Chapter 2.7).[132]

First, racemic propargylic alcohol **89** was prepared by the addition of lithiated TMS-acetylide to a solution 2-bromobenzaldehyde (**14**) in Et_2O at 0 °C (Scheme 77). After stirring for 2.5 h at this temperature, workup and purification by column chromatography the desired product was obtained in 93% yield.



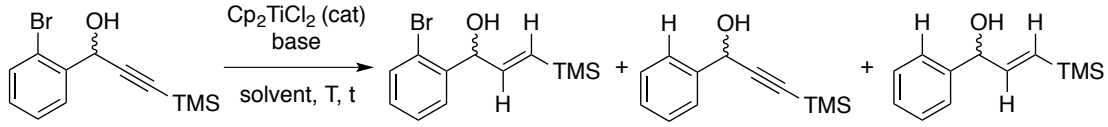
14 **89**

Scheme 77: Synthesis of racemic propargylic alcohol **89**.

With substrate **89** in hand, the hydromagnesiation-magnesiation sequence to form a 1,5-bifunctional organomagnesium reagent **86** was investigated (Table 11). For this, a solution of organometallic reagent, *s*-BuMgBr in Et_2O or *n*-Bu_2Mg in *n*-heptane, was added to a suspension of catalyst Cp_2TiCl_2 in the specified solvent at 0 °C and the black mixture was stirred for 5 min. A solution of propargylic alcohol was added and the reaction mixture stirred for the time specified in Table 11. The reactions were monitored by quenching aliquots with small amounts of water, evaporation of the crude and measurement of ^{1}H-NMR spectra. The integrals of the products of interested were compared and the conversion was calculated qualitatively by dividing the integral of one product through the sum of all the product integrals. After stirring over night with 5 mol% catalyst loading in Et_2O the desired hydromagnesiation was observed, though almost no metalation of the arylbromide (Table 11, entry 1). In THF and 2-MeTHF no hydromagnesiation was observed (Table 11, entry 2 and 3). A higher catalyst loading of 20 mol% led to an increased formation of product **90** in Et_2O, however the reaction slowed down significantly after a short productive initial period (Table 11, entry 4 and 5). Lowering the catalyst loading to 10 mol% and switching to *n*-Bu_2Mg gave a comparable product distribution (Table 11, entry 6). The conversion-rate increased significantly, when the reaction was performed in the non-coordinating solvent toluene, but also here the reaction slowed down and stopped before completion (Table 11, entry 7). Catalyst re-addition allowed further conversion, however not to productive extent and significant conversion

stopped after stirring for one additional hour (Table 11, entry 8). Conducting the reaction at 90 °C for 1 h indicated full metalation, since full conversion to product **92** accompanied with decomposition products was observed (Table 11, entry 9). Workup with D_2O showed about 50% of deuterium incorporation at the olefinic position. Due to further decomposition products, the ^{1}H-NMR did not allow proof, if incorporation and hence successful metalation occurred at the aromatic ring. After the addition of methyl benzoate, no product formation was observed. Lowering the reaction temperature to 50 °C required to elongate the reaction time to 18 h to achieve full conversion to **92**, but also no productive reaction was detected after the ester addition (Table 11, entry 10). Therefore, the preparation of the desired 1,5-bifunctional organomagnesium precursor by hydrometalation seemed not to be a viable approach. In all reactions was observed that, after a short productive period in the beginning, the hydrometalation slowed down significantly and never reached completeness at room temperature. This suggests that the catalyst is probably deactivated and the catalytic activity degrades. With the higher temperatures that allowed full conversion and with longer reaction times broad peaks in the ^{1}H-NMR spectra were detected, suggesting the formation of significant amounts of decomposition products. Interestingly, in retrospect with having the corresponding diol in hand, traces of the desired diol could be found in the crudes of entry 7 and 8 by comparing the ^{1}H-NMR spectra. Considering this, it is likely that the desired reagent is formed, but its decomposition under the applied conditions outcompetes its slow formation. The detected traces of diol are far away from reasonable amounts, however this observation might allow to reinvestigate and optimize the conditions of the hydromagnesiation-magnesiation approach in future studies.

Table 11: Screening to develop a hydromagnesiation-magnesiation sequence to access a 1,5-bifunctional organomagnesium reagent.[a]



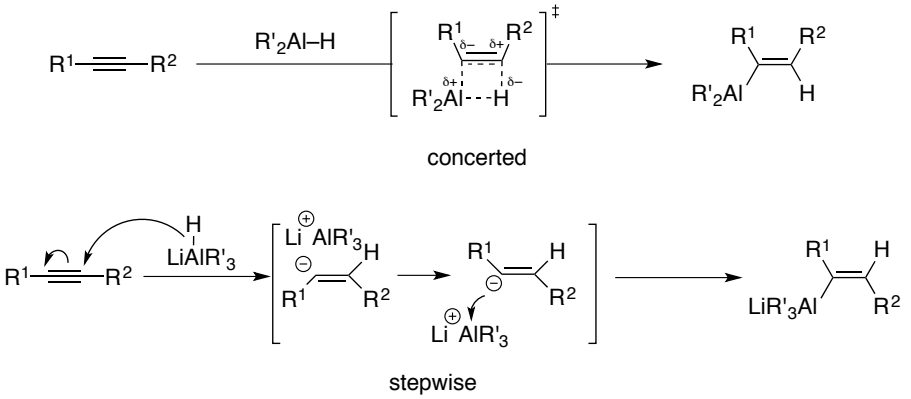
89 **90** **91** **92**

Entry	Catalyst-load	reagent	solvent	T	t	ratio of products **89/90/91/92**
1	5 mol%	*s*-BuMgBr	Et_2O	RT	14.5 h	83:12:5:<1
2	5 mol%	*s*-BuMgBr	THF	RT	12.5 h	85:0:15:0
3	5 mol%	*s*-BuMgBr	2-MeTHF	RT	12.5 h	91:0:9:0
4	20 mol%	*s*-BuMgBr	Et_2O	RT	2 h	80:13:8:0
5					17 h	53:32:11:3
6	10 mol%	*n*-Bu_2Mg	Et_2O	RT	13 h	47:27:21:5
7	10 mol%	*n*-Bu_2Mg	toluene	RT	2 h	56:25:16:3
8	+10 mol%				3 h	29:34:24:13
9	10 mol%	*n*-Bu_2Mg	toluene	90 °C	1 h	0:0:0:100
10	10 mol%	*n*-Bu_2Mg	toluene	50 °C	18 h	0:0:0:100

[a] Reactions performed with 300 µmol of propargylic alcohol **89**. Ratios of **89/90/91/92** determined by ^{1}H-NMR (**89**: δ = 5.79; **90**: δ = 5.59; **91**: δ = 5.45; **92**: δ = 5.19) after quenching aliquots with H_2O and evaporation of solvent.

Hydroalumination

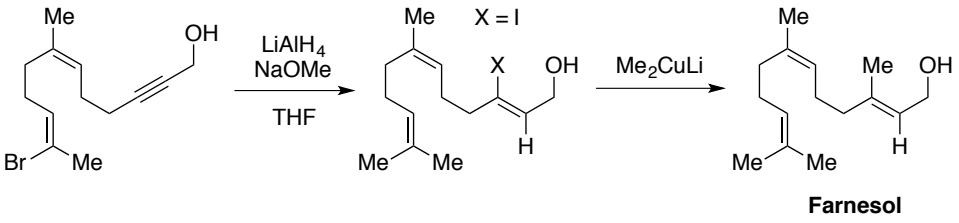
The regioselective hydroalumination of unsymmetrically double substituted alkynes is a well developed methodology to access synthetically useful vinylalane-intermediates, which can be functionalized to tri-substituted olefins.[133] The hydroalumination of alkynes can be stereospecific and gives either *cis* or *trans* olefins. Dialkylalanes (R_2AlH), like for example diisobutylaluminium hydride (DIBALH), react with alkynes in a concerted *syn*-addition, usually resulting in the formation of kinetically favored *cis*-alkenylalanes. Depending on the substrates and conditions applied, these may subsequently isomerize to the corresponding more stable *trans*-products. This isomerization to the thermodynamically more stable *trans*-product is known to be in particular facilitated by silyl-substituents.[134] In contrast, aluminates ($MAlH_4$, MR_3AlH_4) like i.e. trialkylaluminates, $LiAlH_4$ or Red-Al® presumably react with alkynes in a stepwise stereospecific *anti*-addition giving directly *trans*-alkenylaluminates.



Scheme 78: Hydrometalation of disubstituted alkynes: *Syn*-addition of dialkylalanes (R'$_2$Al–H) *via* a concerted mechanism and *anti*-addition of charged aluminates (R'$_3$AlH))*via* a stepwise mechanism.

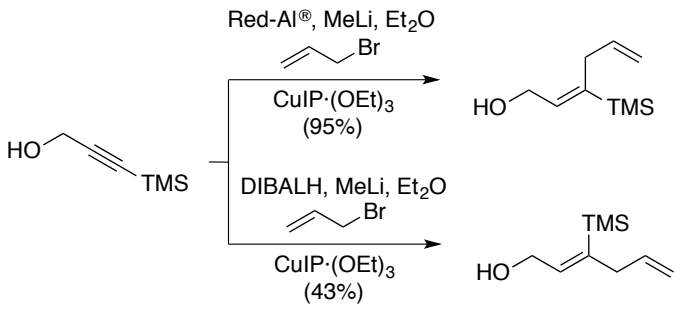
The neutral alkenylalanes are often not nucleophilic enough to react directly with electrophiles and are therefore activated with nucleophiles (e.g. MeLi) to form the more nucleophilic aluminates.[135] In general, the configuration of the double bond of alkenylaluminium compounds is retained, during the transfer of the alkenyl-residue to electrophiles.

In the context of this work, the *trans*-selective hydroalumination of alkynols is desired, which have been investigated before in pioneering natural product syntheses by Corey (Scheme 79).[136] The regio- and stereoselective outcome in the hydrometalation of propargylic alcohols depends significantly on the adjacent hydroxyl-function, and can be influenced by reagents, solvent and protecting groups.



Scheme 79: Corey's total synthesis of farnesol by a *trans*-selective hydroalumination.

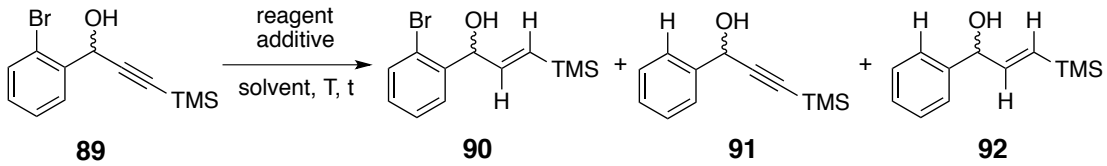
In most studies, the obtained intermediate alkenylaluminium compounds were quenched with iodine to give the corresponding alkenyliodides, which serve as precursor for M–X-exchange reactions. Though, the organoaluminium-intermediates can also directly react with electrophiles (Scheme 80).[137]



Scheme 80: *Trans* and *cis*-hydroalumination-alkylation sequences of propargylic alcohols with allyl bromide developed by Jamison.

Based on this knowledge, the hydroalumination of propargylic alcohol **89** was investigated in detail with the intention to develop a route to prepare a 1,5-dihalo-precursor, which can be metalated in a subsequent step to give a 1,5-bifunctional organomagnesium reagent. In parallel, the possibility to develop a hydroalumination-metalation sequence to give a 1,5-bifunctional aluminate, which is capable to directly react with esters, was envisioned and investigated as an interesting alternative. The reaction of propargylic alcohol **89** with Red-Al®(1.7 eq) in Et_2O at RT for 1 h mainly gave the desired *trans*-reduced product **90** (Table 12, entry 1). Subsequent addition of MeLi and stirring for 15 min indicated metalation of the aryl bromide by the formation of **92**, however quenching the reaction with D_2O and iodine only allowed incorporation respectively functionalization at the vinylic position (Table 12, entry 2). The addition of an aliquot of the reaction mixture to methyl benzoate also did not yield any double-addition product. Next, *i*-Bu_2MeAlH was prepared by mixing DIBALH with MeLi.[138] This mixture was added to a solution of substrate **89** in Et_2O at RT and stirred for 1 h. No reaction was observed, even after addition of Cp_2ZrCl_2 and after elongated reaction time (Table 12, entry 3 and 4). Therefore, the solvent was switched to THF and the reaction conducted at 70 °C, which mainly led to defunctionalization of the aryl bromide giving product **91** (Table 12, entry 5 and 6). Also the addition of diglyme, which was added with the intention to form a more reactive aluminate by chelation of the lithium-cation, did not enhance the desired hydrometalation.[139]

Table 12: Screening of conditions for the hydroalumination of propargylic alcohol **89** with the hydroaluminates Red-Al® and *i*-Bu_2MeAlH**.**

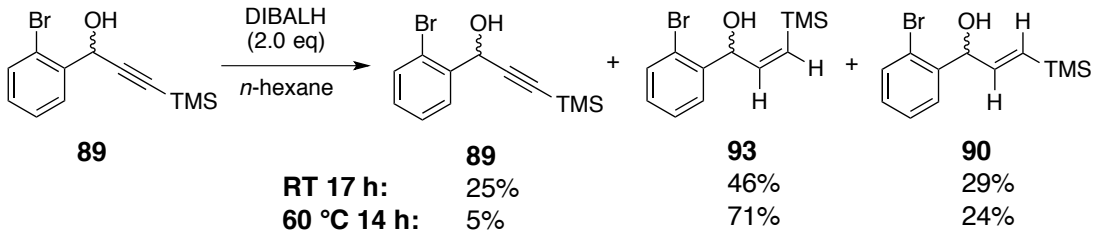


89 **90** **91** **92**

Entry	Reagent	Additive	Solvent	T	t	Ratio of products **89/90/91/92**
1	Red-Al®	—	Et_2O	RT	1 h	4:72:10:14
2	Red-Al®	MeLi	Et_2O	RT	15 min	0:20:4:76
3	*i*-Bu_2MeAlH	—	Et_2O	RT	1 h	100:0:0:0
4	*i*-Bu_2MeAlH	Cp_2ZrCl_2	Et_2O	RT	60 h	95:0:5:0
5	*i*-Bu_2MeAlH	—	THF	70 °C	0.5 h	76:7:17:0
6	*i*-Bu_2MeAlH	—	THF	70 °C	16 h	48:14:34:4
7	*i*-Bu_2MeAlH	diglyme	THF	70 °C	13 h	26:19:44:12

[a] Reactions performed with 300 µmol of propargylic alcohol **89**. Ratios of **89/90/91/92** determined by ^{1}H-NMR (**89**: δ = 5.79; **90**: δ = 5.59; **91**: δ = 5.45; **92**: δ = 5.19) after quenching aliquots with H_2O and evaporation of solvent.

Next, propargylic alcohol **89** was hydrometalated with DIBALH (2.0 eq) in *n*-hexane (Scheme 81). The reaction was slow at RT and after 17 h no full conversion of the starting material was achieved. The main product was found to be the expected *syn*-addition product **93**, but also isomerization to the desired *trans*-product **90** was observed. Conducting the hydrometalation reaction at 60 °C for 14 h allowed higher conversion, however the *cis*/*trans*-product-ratio did not improve. Interestingly, in the reactions with DIBALH, no other side products were observed and the aryl bromide remained untouched under all applied conditions, which is in contrast to the observations made for the reactions with hydroaluminates (cf. Table 12).



89 **89** **93** **90**

RT 17 h: 25% 46% 29%

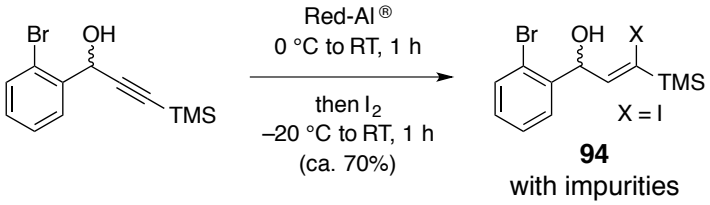
60 °C 14 h: 5% 71% 24%

Scheme 81: Hydrometalation of propargylic alcohol **89** with DIBALH. Scale and conversions determined by ^{1}H-NMR like described in **Table 12** (**93**: δ = 5.68).

In an attempt to form a 1,5-bifunctional aluminate, *n*-BuLi was added at 0 °C and the mixture was stirred for 2 h. A solution of methyl benzoate in THF was subsequently added and the mixture was stirred for 3 h at 60 °C. Intriguingly, in the further course of the project after having a product reference in hand, we found that smallest traces of the desired double addition product were formed in this reaction. This indicates that an aluminate-species in this mixture was capable to undergo a double nucleophilic addition with an ester, however the observed amounts were far from reasonable quantities.

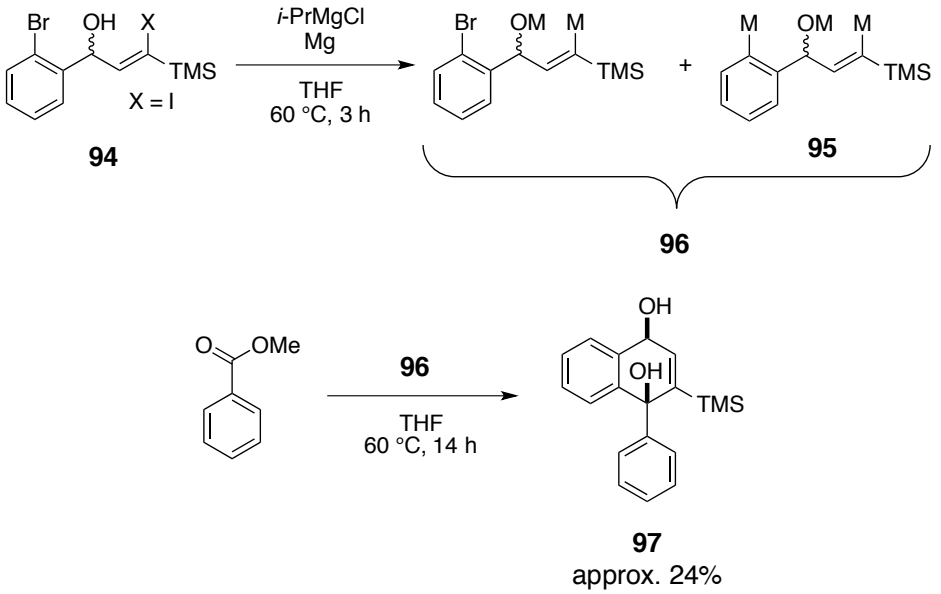
2.8.2 Preparation of a 1,5-Dihalo-precursor, Magnesiation and the First Stereoselective Ester to Diol to Arene Transformation

The hydroalumination-screening revealed that Red-Al® in Et_2O performed best, however did not allow to form a 1,5-bifunctional aluminate that is able to undergo a double nucleophilic addition with esters. Therefore, this reaction was utilized for a first synthesis of a 1,5-dihaloprecursor and the desired product **94** could be obtained after column chromatography in approx. 70% yield, containing about 10% of diverse impurities.



Scheme 82: First preparation of 1,5-dihalo-precursor **94** *via* hydroalumination with Red-Al®.

Partial metalation of impure precursor **94** was achieved at 60 °C in THF after 3.5 h by applying the deprotonation-magnesiation sequence developed in Chapter 2.5. Methyl benzoate was treated with the obtained mixture **96**, containing the racemic 1,5-bifunctional organomagnesium alkoxide reagent **95** and partial conversion from the ester to the corresponding desired racemic diol **97** could be determined in the crude ^{1}H-NMR-spectra after stirring the mixture at 60 °C for 14 h.

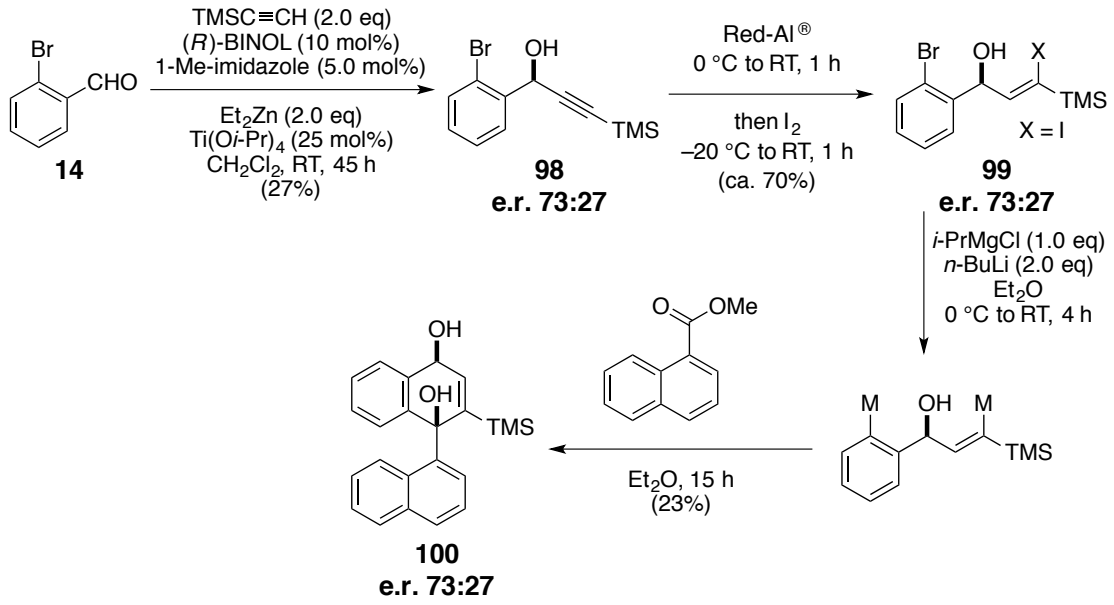


Scheme 83: First magnesiation of dihalo-precursor **94,** followed by the first productive double nucleophilic attack of the corresponding 1,5-bifunctional organomagnesium alkoxide reagent **95** to an ester.

The applied magnesiation protocol did not allow a complete magnesiation in following experiments, since elongation of the reaction time led to reagent decomposition and the subsequent reaction with methyl benzoate gave inferior results. Nonetheless, for the first time, a 1,5-bifunctional organometallic-alkoxide reagent was formed, which underwent a double nucleophilic attack to a substantial extent and allowed access to the desired racemic *cis*-diols. This set the stage to investigate, if a central-to-axial chirality conversion can be realized in the context of a direct ester to naphthalene transformation.

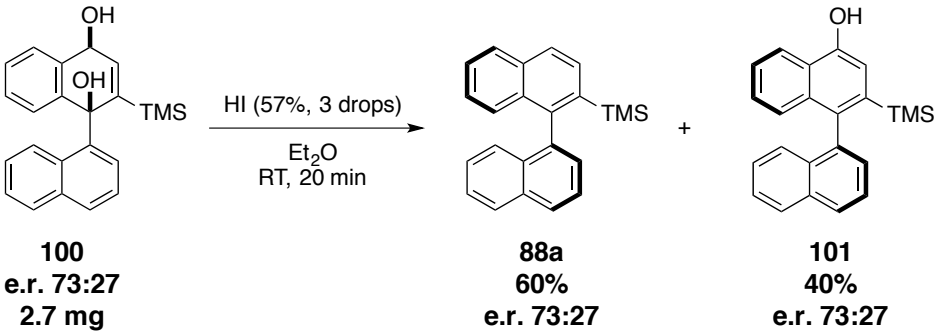
First Stereoselective Ester to Naphthalene Transformation

The direct stereoselective alkynylation[140] of 2-bromobenzaldehyde **14** gave enantioenriched propargylic alcohol **98** in 27% yield and an e.r. of 73:27 (Scheme 84). Following hydrometalation with Red-Al® as described in Scheme 82 proofed to be reliable and delivered the enantioenriched 1,5-dihaloprecursor in enantioenriched form (e.r. 73:27) with retention of configuration. Deprotonation with *i*-PrMgCl followed by metalation with *n*-BuLi allowed, after addition of methyl 1-naphthoate and workup with aqueous NH_4Cl-solution, to obtain the corresponding diol fully stereospecifically with an e.r. of 73:27 in 23% yield.



Scheme 84: The first stereoselective preparation of 1,5-dihalo precursor **99** by direct alkynylation and the stereoselective ester to diol transformation with enantioenriched 1,5-bifunctioal organometallic reagent.

In a preliminary experiment, the enantioenriched diol **100** was then stereospecifically aromatized to the corresponding binaphthalene **88a** by the addition of concentrated hydroiodic acid.



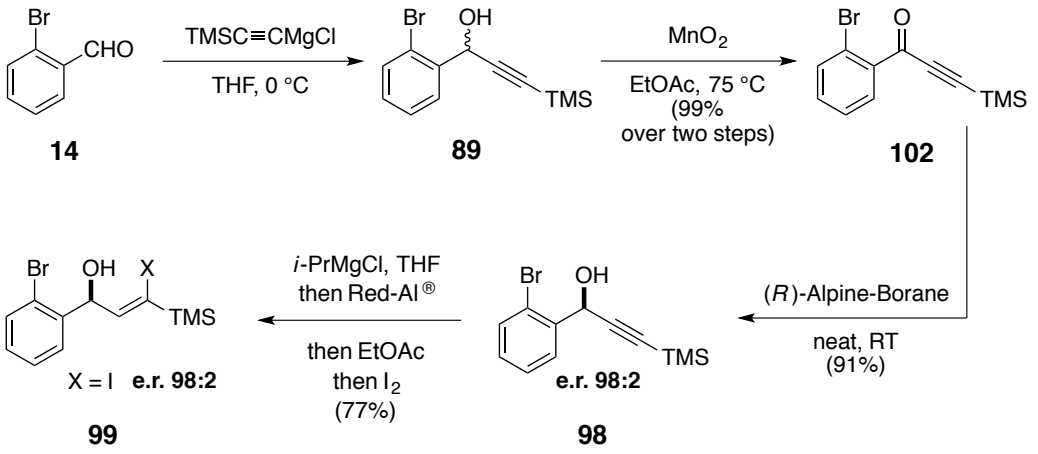
Scheme 85: Stereospecific aromatization to naphthalene **88a** and naphthol **101** by reaction of diol **100** with hydroiodic acid in Et_2O.

This confirmed that the concept to prepare axially chiral naphthalenes by the direct ester to arene transformation via a central-to-axial chirality conversion is feasible.

2.8.3 Second Generation Synthesis of the 1,5-Dihalo-precursor

The preliminary experiments described in the previous two chapters set the stage to develop a highly efficient synthesis of enantioenriched 1,5-dihaloprecursor **99** (Scheme 86). The preparation commenced by deprotonation of ethynyltrimethylsilane with *i*-PrMgCl and addition of the resulting Grignard-reagent to 2-bromobenzaldehyde (**14**) to give racemic propargylic alcohol **89** without the need for purification. Initial attempts to access a highly enantioenriched propargylic alcohol by derivatization to an acid and resolution via crystallization after diastereomeric salt formation with chiral amines were not successful. Resolution attempts by enzymatic acetylation with Novozym 435 (Sigma-Aldrich L4777) failed, since under several conditions no conversion of starting material was observed.[141] Furthermore, the direct stereoselective alkynylation was not effective to access highly enantioenriched material in good yield. Therefore, an oxidation-stereoselective-reduction route was developed.[6] Addition of magnesiated TMS-acetylide and subsequent oxidation with manganese(IV) oxide in hot ethyl acetate for 7.5 h gave 99% over two steps of pure propynone **102** after filtration over a plug of celite. The following Midland-reduction with (*R*)-Alpine-Borane® under neat conditions for 24 h at room temperature yielded 91% of the chiral propargylic alcohol **98** after purification by column chromatography in an enantiomeric ratio of 98:2.[142] Hydroalumination performed best, when propargylic alcohol **98** was deprotonated with *i*-PrMgCl, prior to Red-Al® addition at 0 °C. Furthermore, higher yields were obtained, when an excess of Red-Al® was quenched at low temperature with ethyl acetate previous to the addition of iodine.[143] This gave the desired 1,5-dihaloprecursor **99** in a yield of 77% and in an enantiomeric ratio of 98:2.

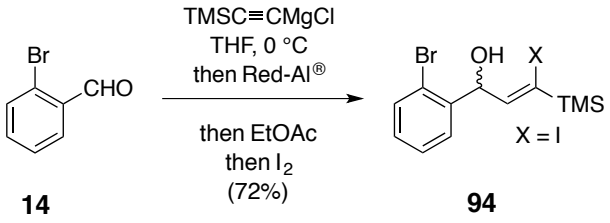
[6] Very recently an efficient Ru-catalyzed asymmetric transfer hydrogenation for the preparation of propargylic alcohol **98** was reported: *Org. Lett.* **2018**, *20*, 975.



Scheme 86: Midland reduction of propynone **102** gave enantioenriched chiral propargylic alcohol **98**, which allowed the synthesis of 1,5-dihalo-precursor **99** with an e.r. of 98:2 *via* hydroalumination.

All starting materials and reagents of the presented synthesis are low-priced and commercially available. The synthesis is performed without the use of halogenated solvents, at high concentrations or neat and is therefore convenient for large scale synthesis with standard laboratory equipment.

The corresponding racemic precursor **94** was prepared by an improved one step alkynylation-hydroalumination sequence. The desired product could be purified without the need of column chromatography by recrystallization in *n*-heptane at high concentrations in a yield of 72%.



Scheme 87: Synthesis of racemic 1,5-dihalo-precursor **94** via an one-step alkynylation-hydroalumination sequence.

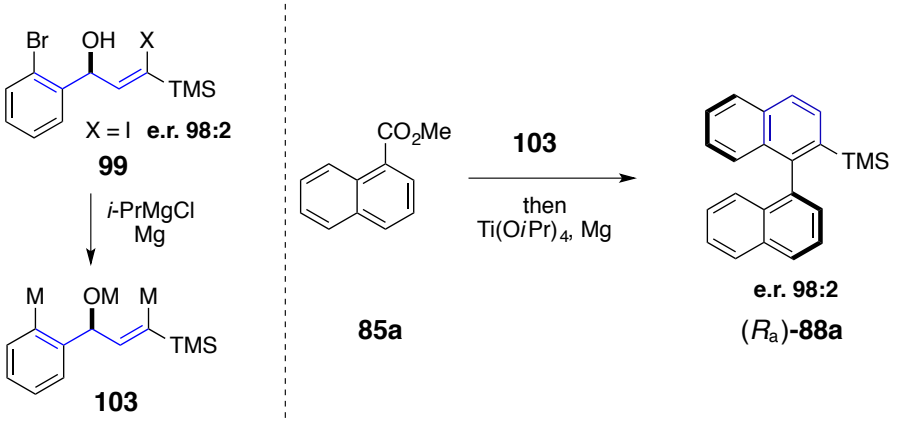
The necessary racemic references of the axially chiral naphthalenes synthesized in the following chapter were prepared from this racemic precursor.

2.8.4 Optimization of the Stereoselective Direct Ester to Chiral Naphthalene Transformation

Having established reliable access to the enantioenriched dihaloprecursor **99** allowed to explore the metalation to form the corresponding 1,5-bifunctional organomagnesium reagent **103** and its direct addition to methyl 1-naphthoate as a model substrate. The following screening builds upon the previously developed deprotonation-magnesiation strategy (see Chapter 2.5). Subsequent addition of $Ti(O\textit{i}\text{-}Pr)_4$ to the reaction mixture performed best for the direct in situ reduction of the intermediary bisalkoxide to the corresponding binaphthalene **88a**.[144] This allowed to investigate, if the central chirality of the reagent-precursor can be efficiently transferred into the chirality axes of the aromatized products **88** in the context of a one-pot reaction design.

The screening started applying the known deprotonation-magnesiation procedure, however magnesium powder (50 mesh) was used instead of freshly cut magnesium pieces to ensure consistent reaction conditions and to enhance the reaction rate.

Table 13: Optimization of the generation of reagent **103**,[a] of the reaction parameters of the double nucleophilic addition to methyl 1-naphthoate[b] and of the in situ reduction to axial chiral binaphthalene (R_a)-**88a**.[c]



Entry	Metalation[a]	Reduction[c]	Yield[d]
1[e]	THF, RT to 60 °C 12 h, 1.5 eq.	—	—
2	THF, 1.5 eq.	THF RT, 1 h	—
3	**Et_2O**, 1.5 eq.	**Et_2O** RT, 1 h	64% of diol 16% of reduced
4	Et_2O, 1.5 eq.	**THF** RT, 1 h	80%
5	**MTBE**, 60 °C 3.5 h, 1.5 eq.	—	—
6	**2-MeTHF**, 1.5 eq.	**2-MeTHF** RT, 1 h	—
7	**Et_2O, 1.25 eq.**	**THF** **RT, 1 h**	**82%**
8	Et_2O, **1.1 eq.**	THF RT, 1 h	79%
9	Et_2O, **RT**, 1.1 eq.	THF RT, 1 h	58%
10	Et_2O, 1.1 eq.	THF **40 °C**, 1 h	73%

[a] Deprotonation of 1,5-dihaloprecursor **99** with equimolar amounts of *i*-PrMgCl. Metalation with 3 mmol of Mg-powder and 640 µmol LiCl at 40 °C for 45 min or under the specified conditions. Solvent and amount of equivalents of **99** in respect to methyl 1-naphthoate as specified. [b] Addition of a solution of 200 µmol methyl 1-naphthoate in 2 mL of the same solvent as specified for the H-M-exchange to the reaction mixture at RT and stirred for 1 h at RT. Entry 10: stirred at 40 °C. [c] Addition of 4 mL of the specified solvent, followed by the addition of 600 µmol $Ti(O$*i*$-Pr)_4$ to the reaction mixture and stirred for 3 h at RT. [d] yield of isolated product. [e] without addition of LiCl.

Hence, addition of *i*-PrMgCl to a slurry of magnesium-powder in THF was followed by addition of a solution of dihaloprecursor **99**. In THF at RT only mono-metalation of the iodo-alkenyl position was observed. After heating the reaction mixture to 60 °C, slow metalation was monitored, however was accompanied with decomposition of the reagent (Table 13, entry 1). Therefore, the reaction temperature was reduced to 40 °C to prevent decomposition pathways and LiCl

was added to enhance the metalation rate (Table 13, entry 2).[14] Complete magnesiation was observed and the 1,5-bifunctional organomagnesium reagent **103** was formed in 45 min. In the course of the exchange-reaction, the color of the solution turned to the characteristic yellow, which was observed during the formation of all 1,5-bifunctional organomagnesium reagents previously investigated. A solution of methyl 1-naphthoate in THF was added and the mixture was stirred for 1 h at room temperature. Ti(O*i*-Pr)$_4$ was added to the reaction mixture to give a black slurry, which indicated the formation of a low-valent titanium species.[144] However, after workup no product formation was observed. Therefore, the solvent was switched to Et_2O (Table 13, entry 3). After the ester addition and stirring for about 5 min the formation of a fine white precipitate was observed, potentially an indication that the intermediary 1,4-bisalkoxide **87a** was formed successfully. Adding Ti(O*i*-Pr)$_4$ to the heterogeneous reaction mixture and stirring for 1 h at room temperature allowed to isolate, after workup with hydrochloric acid (1 molL^{-1}), 64% of the corresponding diol **104** and 16% of the desired axially chiral biaryl **88a**. Analysis with chiral HPLC revealed that the arene was obtained with full stereospecificity with an enantiomeric ratio of 98:2. Speculating that full reduction of bisalkoxide **87a** is prevented by the heterogeneous nature of the reaction mixture, THF was added after the completeness of the 1,2-addition to the ester, but before Ti(O*i*-Pr)$_4$ was added (Table 13, entry 4). This allowed to isolate the desired aromatized product **88a** in a good yield of 80%. The organometallic reagent **103** could not be formed in MTBE, while in 2-MeTHF reagent formation was observed, however no product was obtained after ester addition and reduction (Table 13, entry 5 and 6). The previously applied excess of reagent could be successfully minimized to 1.25 equivalents giving the best yield of 82% (Table 13, entry 7). Even with 1.10 equivalents the desired product was formed with almost the same efficiency, which indicates the high efficiency of the halogen-metal exchange reaction (Table 13, entry 8). Conducting the magnesiation at room temperature resulted in a lower yield of 58% (Table 13, entry 9). Thereby, the best temperature for the halogen-metal exchange was determined to be 40 °C, since this temperature also assured the reliable start of the metalation immediately after addition of the dihaloprecursor. Performing the double nucleophilic addition, as well as the

reduction of the intermediary magnesium-alkoxide at 40 °C reduced the yield to 73% yield, demonstrating that these two transformations are more efficient at room temperature (Table 13, entry 7 versus entry 10). In all reactions described in Table 1 an e.r. of 98:2 was measured, highlighting the efficiency of the central to axial chirality conversion of this novel reaction. The absolute configurations for diol **104** and for chiral naphthalene **88a** were determined by X-ray crystallography (Figure 12).

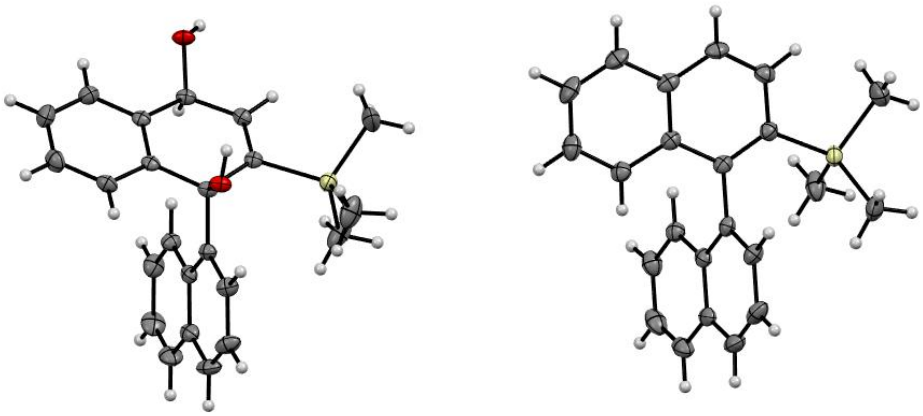


Figure 12: X-ray crystal structures of diol (*S*,*S*)-**104** (CCDC 1820086) and of binaphthalene (R_a)-**88a** (CCDC 1820084).

2.8.5 Scope of the Direct Stereoselective Transformation of Esters into Chiral Naphthalenes

First, the optimized reaction conditions proved to be reliable also in a preparative scale. 2.00 mmol of methyl naphthoate gave 500 mg of the desired aromatized product (R_a)-**88a**, which corresponds to a yield of 77% (Table 14, entry 2). Next, the reaction of chiral 1,5-bifunctional organomagnesium reagent **103** with other methyl esters was explored to develop a direct access to diverse structurally unsymmetric axially chiral biaryls, scaffolds which are difficult to access through methods such as oxidative dimerizations. The methyl group of the *ortho*-tolylester was well tolerated and the desired axially chiral product was obtained with comparable efficiency (Table 14, entry 3). The tetrahydro-naphthalene ester, as well as a 9*H*-fluorene ester were transformed to the corresponding chiral biaryls in good yields and with excellent enantiospecificities (Table 14, entry 4 and 5, 68% and 63%). A sterically encumbered methyl-substituted biphenylester ester could also be converted highly stereospecifically, however the desired product

was obtained in a lower yield of 57% (Table 14, entry 6). The substrate methyl 2-chlorobenzoate demanded to minimize the reduction time after Ti(O*i*-Pr)$_4$ addition from three hours to one hour. This precaution limited dehalogenation to great extent and the corresponding product (R_a)-**88f** could be isolated in a respectable yield of 65% and with full stereoretention (Table 14, entry 7). Next, fluoro-derivative (R_a)-**88g** was obtained in an excellent yield of 78%, however a lower enantioselectivity with an e.r. of 87:13 was observed (Table 14, entry 8). The lower stereoselectivity probably reflects the relative small size of the fluoro-substituent. Therefore, the configurational stability of the product was determined by monitoring the thermal atropisomerization of a solution of the (R_a)-**88g** at 60 °C in *n*-heptane with HPLC and was calculated to be 112 kJmol^{-1}, which corresponds to a racemization half-life of about 4.5 hours. Intriguingly, treating methyl 2-(diphenylphosphino)benzoate with organometallic reagent **103** and reduction for 1 h allowed direct access to the desired axially chiral phosphine (R_a)-**88h** in a synthetically meaningful yield of 63% with an e.r. of 95:5 (Table 14, entry 9). In this case, the lower selectivity is likely to be a result from coordination of the phosphine-group to the metal carried by the intermediary alkoxide during the stereodetermining step, since no product racemization was observed after product isolation. The preliminary assignment of the absolute configuration to R_a is according to the assignment of product (R_a)-**88a** by analogy. Absolute certainty would give determination by X-ray crystallography, but no suitable crystals could be grown yet. Interestingly, by previously deprotonating the protic-group carrying methyl 1*H*-indole-7-carboxylate with *i*-PrMgCl in a separate flask the indole ester could be converted successfully to the corresponding naphthalene (S_a)-**88i** with just 1.25 equivalents of the chiral reagent **103** (Table 14, entry 10). The aromatized product was obtained in a yield of 69% and exquisite stereospecificity with an e.r. of 98:2 was observed. Unexpectedly, the X-ray structure-analysis revealed, that the sterically demanding part is pointing to the front in the representation shown in Table 14, entry 10 and in Figure 13, which is in contrast to the absolute configuration determined for binaphthalene (R_a)-**88a** (see Figure 12).

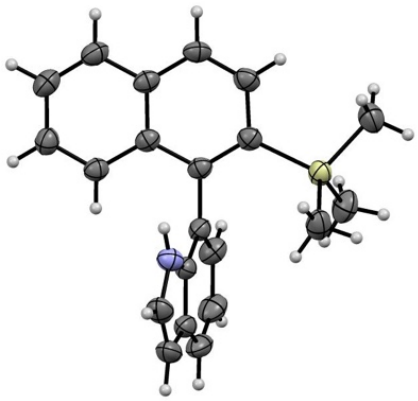
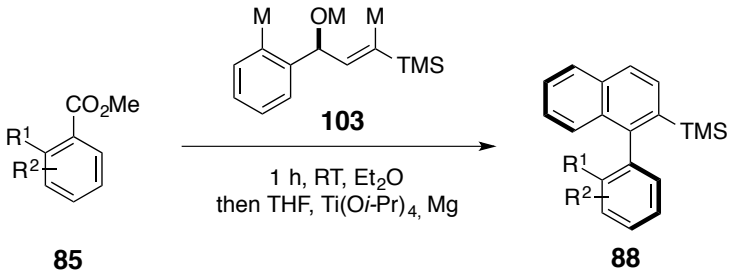


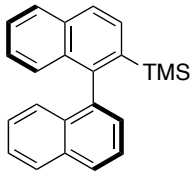
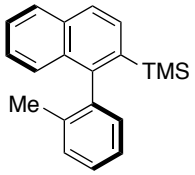
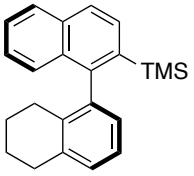
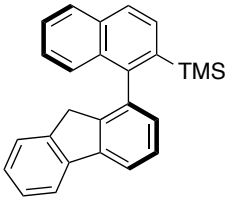
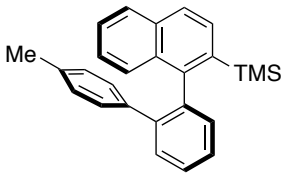
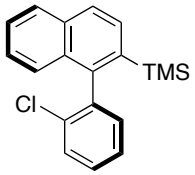
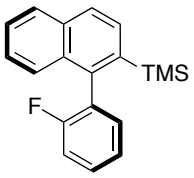
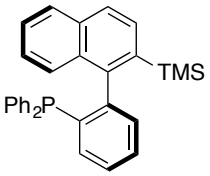
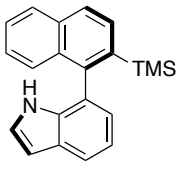
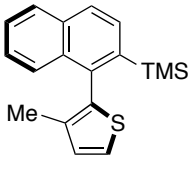
Figure 13: X-ray crystal structure of (S_a)-**88i** (CCDC 1820085), revealing the opposite absolute configuration compared to binaphthalene (R_a)-**88a**.

This observation suggests that the coordination of metal (magnesium or titanium) to the deprotonated nitrogen of the indole and to the oxygen of the intermediary alkoxide in the stereodetermining step is capable to completely inverting the stereoselectivity of the described reaction. The method is also efficient to convert 5-membered heteroaromatic substrates like exemplified by the stereospecific and high yielding synthesis of methyl-substituted thiophene derivative (S_a)-**88j** (Table 14, entry 11, 80%). In a previous experiment an e.r. of 92:8 was observed, which could be increased to an e.r. of 95:5 by evaporating the solvent under reduced pressure at room temperature instead of at 40 °C. This suggests that the lower stereoselectivity observed is the result of a relative low rotational barrier. Subsequently, a rotational barrier of 115 kJmol^{-1} at 60 °C was determined. Also for this substrate the absolute configuration is assigned by analogy, but could be affected by coordination of the heteroatom.

Table 14: Substrate Scope of the direct stereoselective transformation of esters into unsymmetric axially chiral naphthalenes.[a]



85 **88**

Entry	Product	Yield[b]	Entry	Product	Yield[b]
1–2	 (R_a)-**88a**	82% 77%[c] e.r. 98:2 $[\alpha]_D$ +81.0	3	 (R_a)-**88b**	80% e.r. 98:2 $[\alpha]_D$ +52.8
4	 (R_a)-**88c**	68% e.r. 98:2 $[\alpha]_D$ +58.6	5	 (R_a)-**88d**	63% e.r. 97:3 $[\alpha]_D$ +167.9
6	 (R_a)-**88e**	57% e.r. 97:3 $[\alpha]_D$ +101.7	7[d]	 (R_a)-**88f**	65% e.r. 98:2 $[\alpha]_D$ +62.6
8	 (R_a)-**88g**	78% e.r. 87:13 $[\alpha]_D$ +10.1	9[d]	 (R_a)-**88h**	63% e.r. 95:5 $[\alpha]_D$ +71.2
10[e]	 (S_a)-**88i**	69% e.r. 98:2 $[\alpha]_D$ –41.5	11	 (S_a)-**88j**	78% e.r. 95:5 $[\alpha]_D$ +10.6

[a] Reaction performed with 200 µmol ester and chiral 1,5-bifunctional organomagnesium reagent **103**, according to the method described in Table 13, entry 7. [b] Isolated yield; enantiomeric ratio determined by HPLC on a chiral stationary phase; specific rotation measured at 296 K in $CHCl_3$ with c 0.50, entry 1 with c 1.00 (details see experimental). [c] Scale of 2.00 mmol. [d] Reduction conducted for 1 h, instead of 3 h. [e] The protic group was deprotonated by the addition of *i*-PrMgCl (1.00 eq.) to a solution of ester in Et_2O (2.00 mL) in a separate vial, prior to the addition to the reaction mixture.

The narrow line between a product with a rotational barrier sufficiently high to allow the selective preparation by this mild method at room temperature and a product with freely rotating moieties is nicely illustrated by the following comparison. The corresponding furan product **88k** was obtained under the same reaction conditions as described in Table 14 in a yield of 50%, accompanied with the corresponding non-reduced diol of 15%. However, in contrast to the chiral thiophene product **88j**, for the furan derivative a specific rotation of zero was measured. The observation of only one peak on the HPLC chromatogram suggest that atropisomerization occurs at room temperature. The difference of the rotational barrier of the two products can be qualitatively explained by comparing the known bond angles of thiophene and furan.[145] The increased size of the sulfur atom, as well as the smaller bond angles of thiophene entail, that the methyl-group is oriented much more in direction of the naphthalene system and therefore the steric hindrance is significantly increased leading to a higher rotational barrier

.

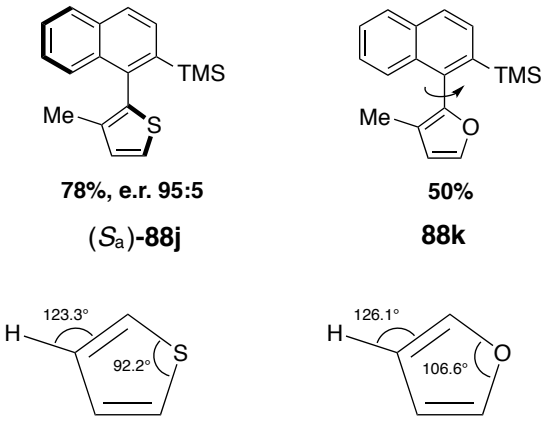
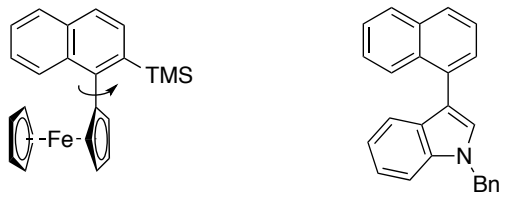


Figure 14: Comparison of configurationally stable thiophene derivative **88j** and the furan derivative **88k**, for which no individual atropisomers were observed in the HPLC time-scale.

Further products, which did not allow to prepare the individual atropisomers are ferrocene-derivative **88l** and the benzyl protected indole-naphthalene **88m** (Figure 15, 57% and 84%). Only one peak was observed for ferrocene **88l** in the chromatogram measured on a chiral stationary phase HPLC, while the indole derivative **88m** showed two separate peaks with the same integral. This suggests fast interconversion in the case of ferrocene-naphthalene **88l**, between the

conformers, which is in accordance to observations made by McGlinchey et al. for comparable ferrocene-systems.[146]

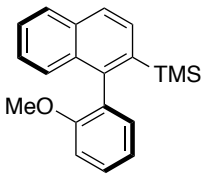


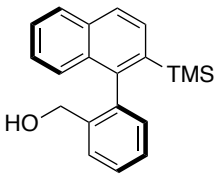
57% **84%, e.r. 50:50**

88l ***rac*-88m**

Figure 15: The ferrocene-derivative **88l** and benzyl protected indole **88m** could not be isolated as individual atropisomers.

The methoxy-containing product **88n** could also be prepared in an acceptable yield of 73% in enantioenriched form, however with lower enantioinduction (e.r. 68:32, Figure 16) compared to the examples described in Table 14. Reduction was conducted with $TiCl_4$ and pyridine as an additive at 60 °C in this case, which gave a much better crude ^{1}H-NMR spectra, than reduction with Ti(O*i*-Pr)$_4$. A reason for the lower stereospecificity might be coordination of the oxygen-atom of the substrate to the metal bound to the alkoxide during the stereodetermining step. But also racemization due to a low rotational barrier of the intermediary alkoxide or of the reduced product and the higher temperature might play a role and ultimately lead to a lower enantiomeric ratio. Therefore, it is not clear which of the atropisomers is the major product and it might be the opposite of the one illustrated. Reduction in a separate step of the corresponding diol, obtained by quenching the Grignard reaction with wet Amberlite IRC-86 and filtration, with a PPh_3–I_2 mixture at RT gave 49% of **88n** in a better enantiomeric ratio of 91:9. Benzylalcohol **88o**, which interestingly could be directly prepared from the corresponding lactone was also prepared by reduction with $TiCl_4$ and pyridine at 60 °C (Figure 16).





$TiCl_4$, pyridine at 60 °C:	**73%, e.r. 68:32**	**61%, e.r. 88:12**
Amberlite IRC 86 wet, *then* PPh_3, I_2 at RT	**49%, e.r. 91:9**	
	88n	**88o**

Figure 16: Synthesis of oxygen-containing products **88n** and **88o** by using $TiCl_4$ and pyridine for the in situ reduction at 60 °C or PPh_3-I_2 in a separate reduction step at RT for **88n**, giving the aromatized products in acceptable yields, but with lower enantioselectivities.

The direct stereoselective ester to axially chiral naphthalene transformations of heterocylic esters **85p** and **85q** (Figure 17) was not efficient and allowed to obtain the corresponding aromatized compounds only in low yields of about 20% to 30%, however the products were still contaminated with significant impurities after purification attempts by column chromatography. The same was experienced for the corresponding product formed from dimethyl protected aniline ester **85r** in about 40% yield. Due to the low yields and impurities, no reliable HPLC nor the specific rotation could be measured for these products. The transformation of esters **85s** and **85t** after deprotonation of their protic-groups with *i*-PrMgCl was not productive. Decomposition under the applied reduction conditions prevented the formation of the desired aromatized products, however clean formation to the corresponding intermediary alkoxides was observed. In the case of *ortho*-bromo ester **85u**, the reduction condition hampered successful product formation by complete dehalogenation. Also the trifluoromethyl-group **85v** was well tolerated in the Grignard reaction, while the reduction led to decomposition. The substrate methyl 2-methyl-1-naphthoate (**85w**) was completely inert to react with 1,5-bifunctional organomagnesium reagent **103**, probably due to the high steric hindrance. After applying the reaction conditions of Table 14 to the esters **85x** to **85χ**, only traces of the potential products or no product formation was observed in the crude reaction mixture. Therefore, no purification attempts were carried out in these cases.

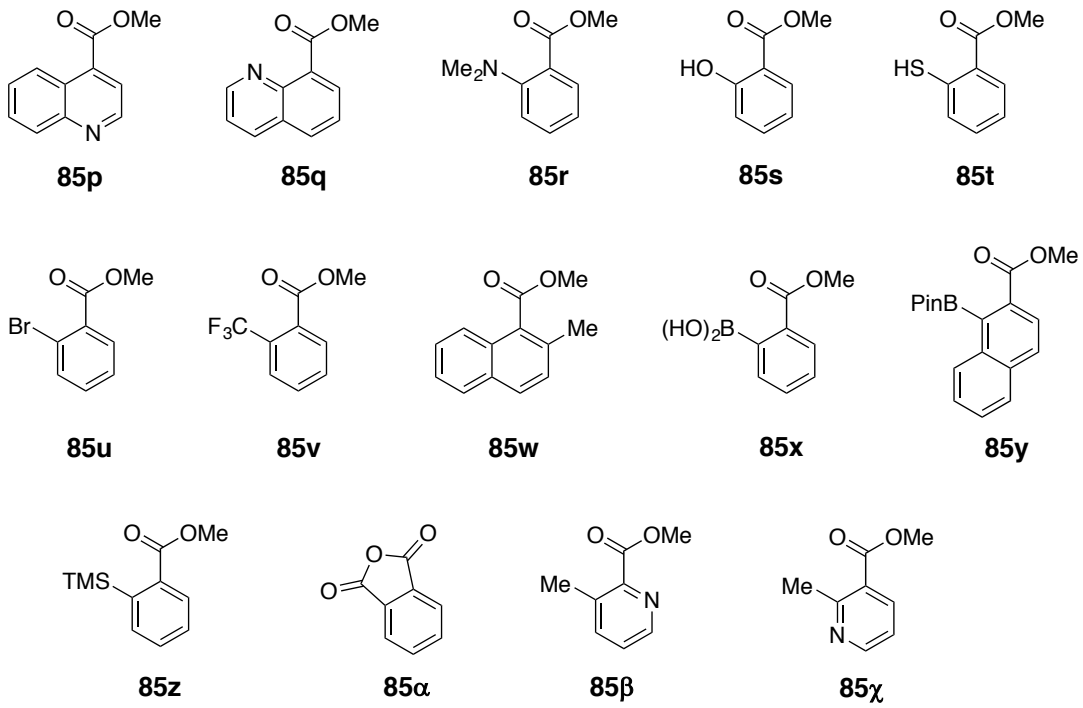
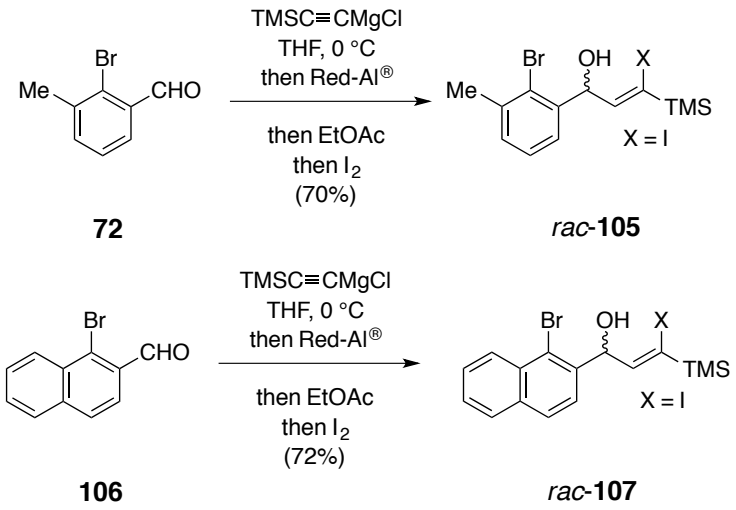


Figure 17: Miscellaneous substrates that did give the aromatized products only in low yields with impurities (**85p** to **85r**); that where converted to the intermediary bis-alkoxide, but decomposed during reduction (**85s** to **85u**); that did not react with the organometallic reagent (**85w**); or that did not yield any isolable amounts of product (**85x** to **85χ**).

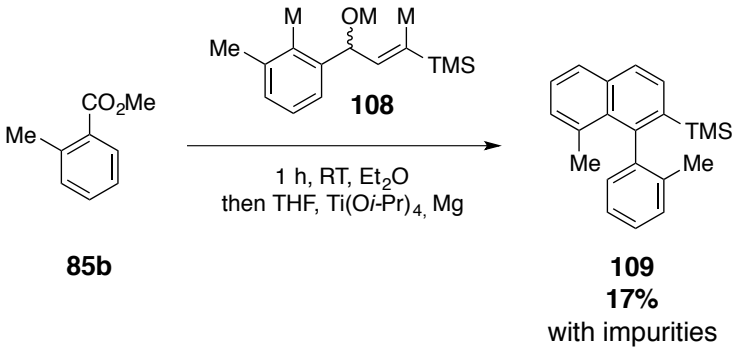
Concluding from these observations, it can be expected that small changes of the reaction parameters, especially of the conditions for the reduction may allow to successfully convert the described esters in the future. Probably in many cases, a successful approach would be to isolate the diol and switch from a one-pot reaction sequence to a two-step procedure.

Two other racemic reagent precursors were prepared with the intention to prepare 8-methyl-substituted naphthalenes and phenanthrenes. These products would show an increased rotational barrier, which might allow to stereoselectively prepare the axially chiral derivatives of e.g. furan **88k** or ferrocene **88l**. In the further course of the project, also other substrates with a low degree of substitution on the ester side might be converted.



Scheme 88: Synthesis of racemic reagent precursors *rac*-**105** and *rac*-**107** to develop a direct ester to 8-methyl-substituted naphthalene and phenanthrene transformation.

Both racemic precursors could be obtained in good yield after recrystallization from a concentrated solution *n*-heptane at –20 °C. Precursor *rac*-**107** was light-sensitive and partially decomposed over one day at room-temperature. A purification attempt by silica gel column chromatography was not successful and led to complete decomposition of the precursor. The same deprotonation-magnesiation conditions as applied before to naphthalene-precursor **99** (see Table 13) allowed the successful metalation of precursor *rac*-**105**, as well as of impure *rac*-**107**. Both formed reagents were reacted with ferrocene ester **85l**, however non of the desired products could be isolated after applying the established conditions for the stereoselective ester to chiral naphthalene synthesis. Also after employment of the more reactive corresponding acid chloride of **85l**, no product formation was observed. Using methyl 2-methylbenzoate (**85b)** did not allow a direct ester to phenanthrene transformation either. However, the reaction of this ester with the methyl-substituted organomagnesium reagent **108** obtained from *rac*-**105** gave the desired methyl-substituted naphthalene **109** in about 17% yield, contaminated with impurities (Scheme 89).

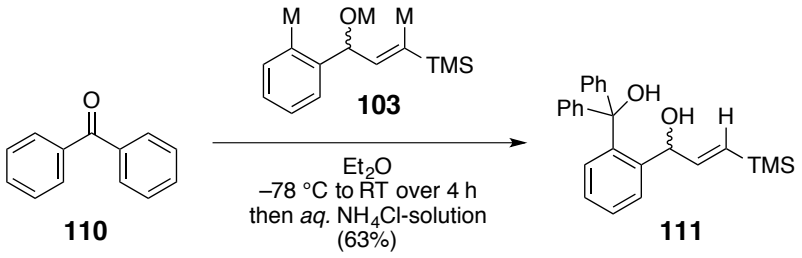


Scheme 89: Preparation of the sterically more congested 8-methyl substituted naphthalene **109**.

This indicates that increased steric hindrance at the 1,5-bifunctional organomagnesium reagent is not well tolerated by the conditions developed for the direct stereoselective ester to chiral naphthalene transformation. Further experiments to improve the yields of the reactions described above have not been attempted.

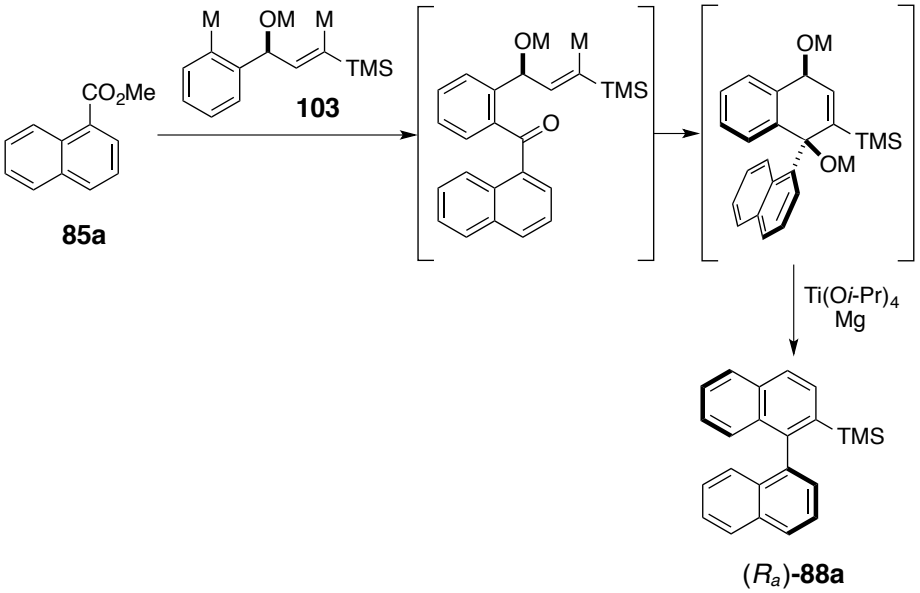
2.8.6 A First Mechanistic Experiment

To get a first idea about the course of the reaction of the unsymmetrical substituted 1,5-bifunctional organomagnesium reagent with an ester and a more precise to answer the question if the vinylic- or the arylic-metalated position attacks first, reagent **103** was reacted with benzophenone (**110**) at –78 °C (Scheme 93). In the following, the reaction mixture was allowed to warm up to room temperature over 4 h. Aqueous workup with a saturated NH_4Cl-solution and purification by column chromatography gave 63% of product **111**, contaminated with unknown impurities.



Scheme 90: Reaction of racemic 1,5-bifunctional organomagnesium reagent **103** with benzophenone at low temperature.

The outcome of this simple experiment is an indication that the 1,5-bifunctional organomagnesium reagent **103** first attacks an ester mainly with the aryl moiety. This result allowed to propose the following more detailed reaction course (Scheme 91).



Scheme 91: Proposal for the course of the reaction of 1,5-bifunctional organomagnesium reagent **103** with carboxylic acid ester **85a**.

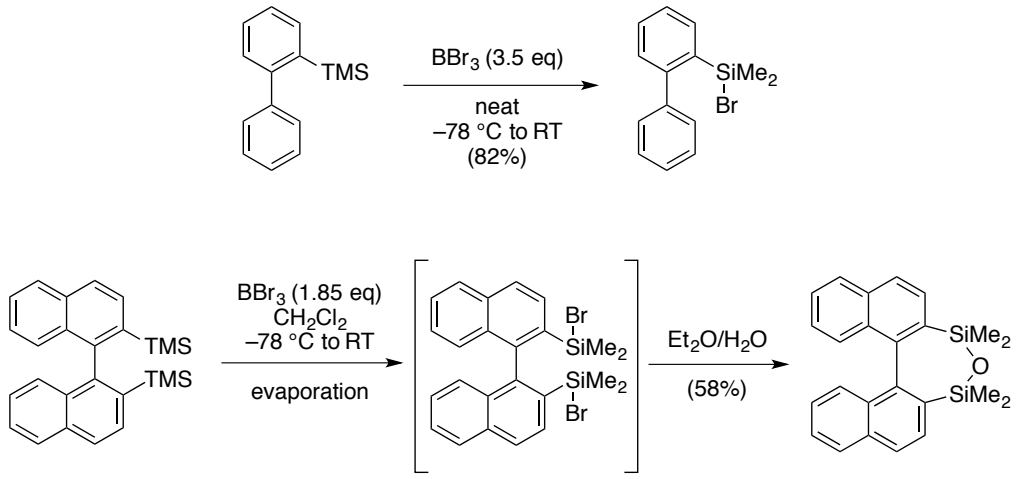
2.8.7 Derivatization of the TMS-substituted binaphthalene

The low cost, low toxicity and high abundance of silicon accompanied with the stability of the C-Si-bond and a distinct reactivity profile compared to traditional organometallics has triggered a broad interest for organosilicon compounds.[147] Arylsilanes are bench-stable and versatile carbanion surrogates, which have a lower reactivity compared to traditional organometallics. Besides the well-established Hiyama-[148] and Hiyama-Denmark-cross-couplings[149] other C–C-bond and C–O-bond forming reactions have been developed such as Au- or Pd-catalyzed couplings, which allow the direct functionalization of relatively unreactive TMS-arenes.[150] Additionally, arylsilanes are utilized as carbanion equivalents in methods where no transmetalation occurs to form new C–C-bonds[147] and further to functionalize aromatics with heteroatoms like sulfur[151], halogens or boron by the *ipso*-substitution of silicon. Based on this, different *ipso*-borondesilylation-metalation-cross-coupling sequences have been developed.[152] The stability and distinct reactivity profiles of arylsilanes allows to realize

divergent synthetic pathways. Recently, chemo- and regioselective catalytic aromatic C–H silylations have been evolved to a powerful tool for the mild late-stage functionalization of pharmaceuticals.[153]

The described stereoselective preparation of chiral arylsilanes in this chapter by the de novo construction of an aromatic ring constitutes a novel way to access these precious compounds and complements known methods. Therefore, different functionalizations of the TMS-group of the axially chiral naphthalene **88a** were explored.

Phenyltrimethylsilane and other trimethylsilyl-substituted benzene derivatives, are known to be easily *ipso*-borylated by boron trihalides in halogenated solvents.[154] The obtained water-sensitive intermediary dihaloboranes can be transformed to the corresponding arylboronic acids and arylboronopinacolates or in-situ coupled with aryl halides under typical Suzuki-Miyaura coupling conditions.[152] Nevertheless, Kaufmann *et al*. reported that treatment of 2-(trimethylsilyl)-biphenyl and 2,2'-bis(trimethylsilyl)-1,1'-binaphthyl with boron tribromide cleaves mainly one C_{Me}–Si-bond giving the corresponding intermediary (bromodimethylsilyl)-derivatives (Scheme 92).[155] Followed by a basic workup this cleavage would allow to obtain silanolates, which are ideal substrates for a subsequent direct functionalization with haloarenes by a Hiyama-Denmark coupling.

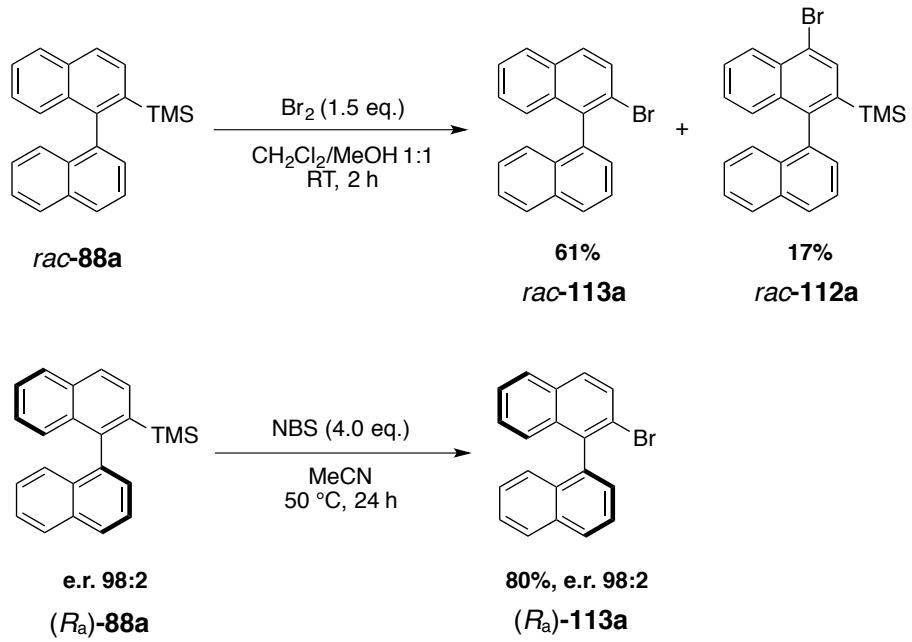


Scheme 92: The literature-known activation of *ortho*-TMS-substituted biaryls by cleavage of a C_{Me}–Si-bond via methylborylation as reported by Kaufmann and coworkers.

With this in mind, the described conditions were applied to substrate (R_a)-**88a**. However, following exactly the described procedure, as well as changing reaction parameters such warm-up time, solvent or reagent did not yield any desired product. Instead, when BBr_3 was employed as the reagent, defunctionalization, i.e. protodesilylation of the substrate (R_a)-**88a** was observed. The speculation that the BBr_3 used from an old bottle might contain HBr, which could be responsible for the defunctionalization, could not be confirmed. When a brand-new high purity containing BBr_3 (>99.99%) ampule was freshly opened and the reagent directly employed, the same defunctionalization was observed. With BCl_3 in CH_2Cl_2, first stirred at room temperature and then in a pressure tube at 80 °C for 6 h no reaction was observed. The same was detected after stirring a mixture of staring material (R_a)-**88a** in *n*-heptane with BCl_3 in a pressure tube at 120 °C for 3 h.

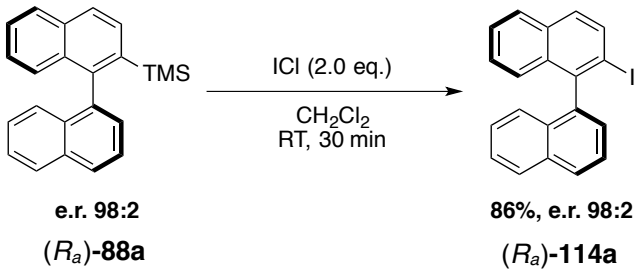
A palladium-catalyzed desilylative acyloxylation described by Kitamura for other TMS-arenes[156] did not yield any of the acetyl-protected naphthol, probably due to steric hindrance.

The addition of bromine to a solution of *rac*-**88a** in CH_2Cl_2 resulted in no reaction. Interestingly, when MeOH was added to this solution rapid conversion was observed.[157] Besides traces of starting material, the desired racemic 2-bromo-1,1'-binaphthalene (*rac*-**113a**) was isolated in a yield of 61%, accompanied with side-product *rac*-**112a** in 17% yield (Scheme 93). Lowering the temperature and changing other reactions parameters did not improve the reaction outcome. Finally, bromination of enantiopure (R_a)-**88a** with NBS in acetonitrile at 50 °C for 24 h was the superior method giving 2-bromo-binaphthalene (R_a)-**113a** in 80% yield and an e.r. of 98:2. (Scheme 93)[158]



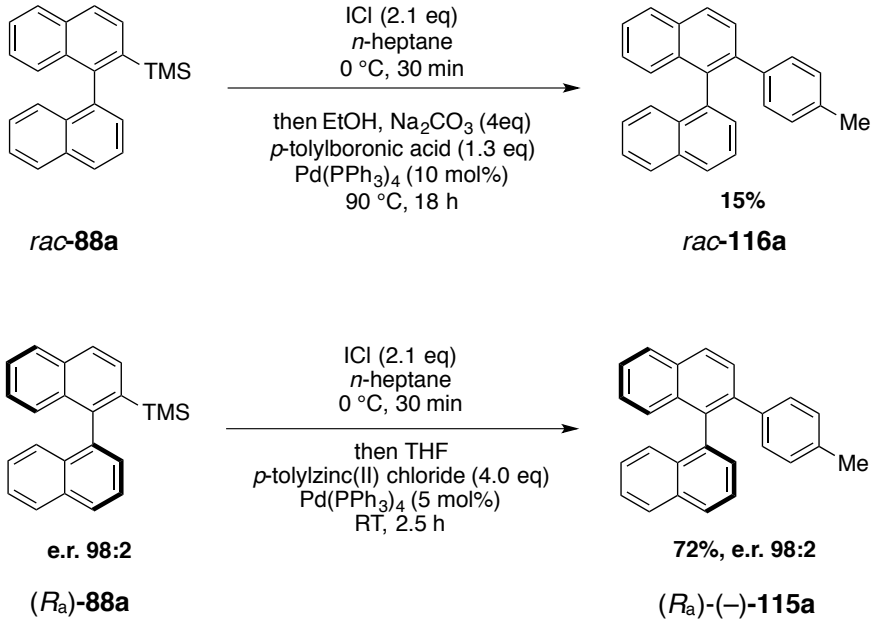
Scheme 93: Functionalization of axially chiral naphthalene **88a** by bromodesilylation with bromine in CH_2Cl_2/MeOH and with NBS in acetonitrile.

Next, the direct iodination of (R_a)-**88a** was achieved by the addition of two equivalents of iodine-monochloride to a solution of substrate in CH_2Cl_2 (Scheme 94).[159] The mixture was stirred for 30 min and after workup and purification by chromatography 86% of (R_a)-2-iodo-1,1'-binaphthalene ((R_a)-**114a**) was isolated. No formation of side products was observed, but incomplete conversion of starting material. However, variation of reactions conditions such as concentration, temperature and equivalents of reagent did not improve the reaction outcome.



Scheme 94: Efficient iododesilylation of (R_a)-**88a** with iodine-monochloride to give (R_a)-2-iodo-1,1'-binaphthalene ((R_a)-**114a**).

Recognizing the high efficiency of this iodination-protocol the development of a mild iodination-cross-coupling sequence was subsequently envisioned. (Scheme 95) First, an iodination Suzuki-coupling was envisaged and for this reaction, an appropriate solvent with a higher boiling point had to be found. An attempt to perform the reaction-sequence in toluene was not successful and revealed that already at room temperature the strong electrophilic iodine-monochloride iodinates the solvent in *para*-position to the methyl-group. Iodination attempts of **88a** in MeOH, EtOH and dimethoxyethane showed no conversion, however iodination with 2.1 equivalents of iodine-monochloride in *n*-heptane showed the same conversion as observed before in CH_2Cl_2. The purple colored reaction solution was then added to a mixture of *p*-tolylboronic acid (1.3 eq.), Na_2CO_3 (4.0 eq.) and $Pd(PPh_3)_4$ (10 mol%) in EtOH and the resulting reaction mixture was heated to 90 °C for 18 h. After purification by chromatography, 15% of the desired product could be isolated. Performing the reaction at 70 °C or 100 °C gave inferior results.



Scheme 95: Iodination-Negishi-cross-coupling sequence for the direct functionalization of TMS-binaphthalene (R_a)-**88a**.

Due to the observed slow reaction rates even at these elevated temperatures, the cross-coupling with *p*-tolylzinc(II) chloride was investigated next. This approach was supported by known efficient and stereoconservative Negishi-cross-coupling protocols for the corresponding 2,2'-diodo-1,1'-binaphthalene reported by Kappe

and Putala.[160] After iodination in *n*-heptane like described before, the Negishi-coupling in THF at 60 °C for 1 h allowed to isolate 66% of the desired (R_a)-2-(*p*-tolyl)-1,1'-binaphthalene ((R_a)-**116a**). Reaction at RT for 2.5 h with 5 mol% of $Pd(PPh_3)_4$ and 4.0 equivalents *p*-tolylzinc(II) chloride gave 72% of product (R_a)-**116a** with an e.r. of 98:2 (Scheme 95). Hence, a direct in situ functionalization of TMS-binaphthalene (R_a)-**88a** with full retention of the configuration by a cross coupling was feasible.

A future prospective, to broaden the opportunities for direct functionalizations of the obtained arylsilanes, is to change the TMS-group to a more reactive silyl-group i.e. to prepare an alternative reagent-precursor from the corresponding alkynylsilane.

3 Conclusion and Outlook

In summary, a strategy for the direct transformation of carboxylic acid esters into various arene derivatives by the reaction with different 1,5-bifunctional organomagnesium reagents has been developed. Furthermore, a novel chiral organomagnesium reagent was designed and applied for the stereospecific synthesis of axially chiral naphthalenes in the context of the direct ester to arene transformation.

3.1 Benzenes and Acenes

The access to a dialkenylmagnesium reagent generated in situ by iodine-magnesium exchange with a lithium trialkylmagnesiate allowed to synthesize aryl-, heteroaryl-, alkyl- and alkenyl-benzenes in yields of up to 82%.

The corresponding diarylmagnesium reagents were prepared with metallic magnesium from the *o*,*o*'-dibromodiarylmethane precursors. The diarylmagnesium reagents enabled the very effective synthesis of anthracenes, tetracenes and pentacenes at room temperature in a single step with yields of up to 99%.

The synthesis of naphthalenes and phenanthrenes by the reaction of 1,5-alkyl-aryl-magnesium reagents and a following in situ 1,2-elimination was not successful. Attempts to metalate the naphthalene-precursor led to decomposition, while the phenanthrene reagent did not react productively with carboxylic acid esters.

3.2 Disubstituted Anthracenes, Anthrone and Phenol

The development of a deprotonation-magnesiation sequence gave access to a 1,5-bifunctional dimagnesiumdiarylmethoxide. Treatment of methyl benzoate with this alkoxide reagent and variation of the acidic workup conditions allowed the synthesis of various di- and mono-substituted anthracenes and anthrones. Intriguingly, workup with diluted HCl gave the corresponding *cis*-diol in 99% yield

as a single diastereoisomer. This outcome presumably results from coordination of the alkoxide metal to the ester carboxyl oxygen during the double nucleophilic addition.

Attempts to synthesize phenols with a corresponding pentadiene Grignard-alkoxide reagent were less successful. Deprotonation, iodine-magnesium exchange with trialkylmagnesiate and reaction with methyl anisate allowed to isolate the desired phenol product in 12% yield, however contaminated with impurities. No reactive Grignard reagent could be obtained by double hydromagnesiation of a bisalkyne precursor.

3.3 The Stereoselective Ester to Arene Transformation

Soon after the start of the project we envisioned to develop a stereoselective ester to arene transformation.

The initial observation that catalytic amounts of quaternary ammonium salts activate 1,5-bifunctional organomagnesium reagents evoked the question, if chiral ammonium salts could catalytically induce stereoselectivity. However, no stereoinduction was observed with diverse chiral additives in the reaction of a non-symmetric organomagnesium reagent with methyl 1-naphthoate and the axially chiral anthracene product was obtained as racemic mixture in every case.

The intriguing observation that the coordination of the alkoxide metal of a bifunctional Grignard reagent to the ester carboxyl oxygen even at high temperatures exclusively forms one diastereoisomer inspired us to develop a chiral organomagnesium alkoxide reagent. We envisioned to prepare the chiral organomagnesium reagent in one step from a chiral bromo-aryl substituted propargylic alcohol by titanium-hydride catalyzed hydromagnesiation. However, defunctionalization of the arylbromide was observed. Therefore, the corresponding dihaloprecursor was prepared in an efficient hydroalumination-iodination sequence. The organomagnesium reagent was prepared by deprotonation with *i*-PrMgCl and direct magnesium insertion in the presence of LiCl.

Treatment of diverse sufficiently substituted non-symmetric esters and in situ reduction over magnesium by addition of Ti(O*i*-Pr)$_4$ enabled to prepare various axially chiral TMS-naphthalenes in one step.

The stereochemical information of the chiral reagent is efficiently transferred into the stereogenic axis of the products by means of a central to axial chirality conversion. The TMS-naphthalenes were obtained in high yields and in most cases with full stereospecificity (82%, e.r. 98:2). Furthermore, the mild reaction conditions at room temperature allowed to prepare two derivatives with low rotational barriers with good stereospecificity. Interestingly, the deprotonated nitrogen of an indole substrate was found to coordinate to the oxygen of the intermediary alkoxide in the stereodetermining step, which completely reversed the stereoselectivity of the described reaction.

Studies on the reactivity, stability and structure of the chiral bifunctional organomagnesium alkoxide reagents as well as preparing corresponding derivatives and developing alternative reduction methods holds promise to expand the stereoselective ester to arene reaction. This may allow to develop this methodology to a reliable and flexible strategy to access desired axially chiral compounds or other products with other chiral entities in future.

4 Experimental Section

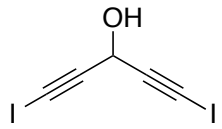
Parts of this Experimental section were published in the supporting information data of the articles listed on page VII.

General Methods:

All chemicals were reagent grade and used as supplied unless stated otherwise. All reactions were carried out in dried glassware under an argon atmosphere. Solvents for extractions and chromatography were technical grade and distilled prior to use. Solutions of *i*-PrMgCl in THF or Et_2O were purchased from Sigma Aldrich or Acros Organics. The concentrations were determined by titration with 1,10-phenanthroline in THF against *s*-BuOH according to Eastham and Watson.[161] THF (99.5%, Extra Dry, over Molecular Sieves, Stabilized, AcroSeal®, Code: 348455000) and Et_2O (99.5%, Extra Dry, over Molecular Sieves, Stabilized, AcroSeal®, Code: 364335000) were purchased from Acros Organics. Magnesium powder (99.8%, 50 mesh, Code: 93-1289) was purchased from Strem Chemicals and stored under an argon atmosphere. Magnesium chips (4-30 mesh, Code: 254118) were purchased from Sigma-Aldrich and freshly cut and heated under vacuum prior to use. Extracts were dried over technical grade Na_2SO_4. Analytical thin layer chromatography (TLC) was performed on pre-coated Merck silica gel 60 F_{254} plates (0.25 mm) and visualised by UV, $KMnO_4$ or CAM stain. Flash column chromatography was carried out on Silicycle SiliaFlash P60 (230–400 mesh). Concentration *in vacuo* was performed by rotary evaporation to ~ 10 mbar at 40 °C, drying at ~ 10^{-2} mbar and at RT (caution: some products are volatile). Nuclear Magnetic Resonance spectroscopy (^{1}H NMR and ^{13}C NMR) spectra were recorded on a *Bruker Avance III* 400 MHz, *Bruker Avance III* 500 MHz spectrometer, *Avance III HD* 600 MHz spectrometer and at 298 K in $CDCl_3$ supplied by *Cambridge Isotope Laboratories* (DLM-7TB-100S). Chemical shifts (δ) are reported in ppm relative to tetramethylsilane (0.00 ppm). The multiplicities are reported in Hz as: s = singlet, br = broad singlet, d = doublet, t = triplet, q = quartet and m = multiplet. High Performance Liquid Chromatography (HPLC) was performed on a Thermoscientific Dionex Ultimate 3000 equipped with a UV-detector and with the chiral column as stated in the individual experiments. Gaschromatography (GC-MS) was performed on a Thermoscientific Trace 1300 Gas Chromatograph with a ISQ single quadrupole MS. Optical rotations were measured at 296 K on s Jasco P-2000 digital polarimeter with a path length of 10.0 cm, using the 589.3 nm D-line of sodium. Concentrations are quoted in g/100 mL. Melting points (m.p.) were measured on a *Büchi B-545* or *a M-565* melting point apparatus in open capillaries and are uncorrected. Infrared Spectroscopy (IR) spectra were measured on a ATR *Varian Scimitar 800* FT-IR spectrometer and reported in cm^{-1}. The intensities of the bands are reported as: w = weak, m = medium, s = strong. High-resolution mass spectrometry (HR-ESI-MS) was performed by Dr. Heinz Nadig of the University of Basel on a *Bruker maXis 4G* QTOF ESI mass spectrometer. X-ray crystallography for structure determination was performed by Dr. Markus Neuburger on a *Bruker Kappa Apex 2* or a *Stoe StadiVari* diffractometer.

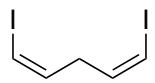
Reagent Preparation (Benzenes)

1,5-Diiodopenta-1,4-diyn-3-ol (7):[103, 104]



To a solution of ethynylmagnesium bromide in THF (800 mL, 0.500 molL^{-1}, 400 mmol) at 0 °C was added ethyl formate (16.8 mL, 198 mmol) over 20 min and the reaction mixture was stirred for 13 h at RT. An aqueous saturated solution of NH_4Cl (120 mL) and H_2O (120 mL) was added. The mixture was extracted with Et_2O (2 x 200 mL), the combined organic phases were washed with brine (100 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was added to a mixture of *N*-iodosuccinimide (93.6 g, 416 mmol) and $AgNO_3$ (3.36 g, 19.8 mmol) in acetone (800 mL) at RT and stirred for 1 h. The solvent was removed *in vacuo*, Et_2O (500 mL) was added and the precipitate was removed by filtration (glass frit with pore size: P16). The filtrate was sequentially washed with H_2O (50 mL) and brine (100 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* (60 °C, 13 mbar) to give a brown solid (61.1 g, 93% over 2 steps). An aliquot was purified by chromatography (Et_2O:pentane 1:4) to obtain a beige solid (decomp. at 147.7 °C): R_f 0.23 (Et_2O: pentane 1:4); ν_{max} (neat): 3174m, 2852w, 2360w, 2326w, 2180m, 2049w, 1614w, 1469m, 1375m, 1271m, 1166w, 1056s, 1019s, 904s, 664s; ^{1}H NMR (500 MHz, $SO(CD_3)_2$) δ = 5.31 (1H, s, C3*H*), 6.31 (1H, br, O*H*); ^{13}C NMR (125 MHz, $SO(CD_3)_2$) δ = 91.4 (*C2*, *C4*), 53.2 (*C3*), 11.8 (*C1*, *C5*); ESI-MS: m/z calcd. for $C_5H_2I_2NaO^+$ 354.8087 found 354.8085 [M+Na$^+$].

(1*Z*,4*Z*)-1,5-Diiodopenta-1,4-diene (1a): [105, 106]



To a solution of 1,5-diiodopenta-1,4-diyn-3-ol (14.9 g, 45.0 mmol) in MeOH (60 mL) was sequentially added pyridine (27.2 mL, 338 mmol) and potassium azodicarboxylate (21.9 g, 113 mmol). AcOH (12.9 mL, 225 mmol) was added over 1.5 h via a syringe pump, while the temperature was maintained at RT. The reaction was stirred for 70 h at RT. Additional potassium azodicarboxylate (4.37 g, 22.5 mmol) and AcOH (2.58 mL, 45.0 mmol) was added and the mixture was stirred for 3 h at RT. Aq. HCl (5%, 100 mL) was added and the mixture was extracted with Et_2O (3 x 150 mL). The organics were washed with brine (100 mL), dried over Na_2SO_4 and the solvents were removed *in vacuo*. The residue was

filtered through a short column of SiO_2 (Et_2O: pentane 1:1; R_f 0.40) to give a yellow liquid (9.93 g). The product was dissolved in CH_2Cl_2 (100 mL) and triethylsilane (9.46 mL, 59.2 mmol) and trifluoroacetic acid (9.07 mL, 118 mmol) were sequentially added at 0 °C. The mixture was stirred at 0 °C for 45 min, an aqueous saturated solution of $NaHCO_3$ (100 mL) was added at 0 °C and the mixture was vigorously stirred for 10 min. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 50 mL). The combined organics were washed with brine (50 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo* (product volatile and temperature sensitive! 400 mbar, 30 °C). The residue was purified by chromatography (pentane) and the fractions were analyzed by GC/MS. The solvent was removed *in vacuo* (1h at 800 mbar 30 °C !, then 13 mbar 30 °C) to obtain a purple liquid (6.54 g, 45% over two steps): The product is stable for at least 1 month in freezer and sensitive to light; R_f 0.54 (pentane); ν_{max} (neat): 3064w, 2991w, 2359w, 1682w, 1612m, 1422w, 1294s, 1257s, 1197m, 1020w, 977w, 936w, 894w, 671s, 623s; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.37 (2H, dt, ^3J 7.40, ^4J 1.48, C1*H*, C5*H*), 6.23 (2H, dt, ^3J 7.31, 6.90, C2*H*, C4*H*), 3.01 (2H, tt, ^3J 6.85, ^4J 1.48, CH_2) ^{13}C NMR (125 MHz, $CDCl_3$) δ = 136.8 (*C2*, *C4*), 84.3 (*C1*, *C5*), 40.7 (*C3*); in agreement with literature data.[100]

(*Z*,*Z*)-1,4-Pentadien-1,5-diyl-Reagent (2):

To a solution of isopropylmagnesium chloride in THF (110 µL, 1.82 mol L^{-1}, 200 µmol) at −20 °C was added additional anhydrous THF (200 µL) and *n*butyllithium in hexanes (294 µL, 1.36 molL^{-1}, 400 µmol). The mixture was stirred at −20 °C for 10 min and a solution of diiodide **1a** (64.0 mg, 200 µmol) in anhydrous THF (1.00 mL) was added at −20 °C. The reaction mixture was stirred at the same temperature for 5 min and the reagent was used directly in the next step.

For **5a** and **5i** 300 µmol isopropylmagnesium chloride in THF, 600 µmol *n*-butyllithium in hexanes and 300 µmol of diiodide **1a** were used.

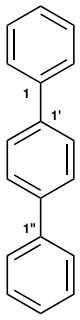
General Procedure A:

To a solution of reagent **2** (prepared as described from 200 µmol **1a** if not stated otherwise) was added a solution of carboxylic acid ester (100 µmol) in anhydrous THF (1.00 mL) at −20 °C and the reaction mixture was stirred at the same temperature for 2 h. Aqueous HCl (1.00 mL, 1.00 molL^{-1})

was added, the mixture was allowed to warm to RT and was extracted with Et_2O (6 x 1.0 mL). The organic layers were washed with brine (1.0 mL), dried over Na_2SO_4 and the solvent was carefully removed *in vacuo* (temperature and pressure specified). The residue was purified by the specified method to yield products **5a-i**.

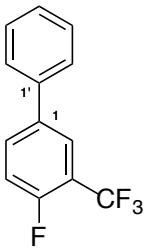
Ester to Benzene Transformation

1,1':4',1''-Terphenyl (5a):



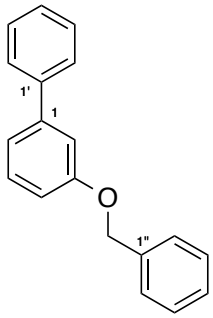
Prepared according to general procedure **A** using methyl 4-phenylbenzoate (21.2 mg, 100 µmol), removal of impurities at 80 °C for 2h and sublimation of product at 140 °C for 30 min (18.9 mg, 82%, m.p. 200.8–202.1 °C): R_f 0.22 (pentane); ν_{max} (neat): 3060w, 3033w, 2959w, 2929w, 2871w, 2361w, 1952w, 1890w, 1681w, 1601w, 1478s, 1455m, 1404m, 1261w, 1190w, 1169w, 1103w, 1076m, 1027m, 1002m, 911w, 838s, 742s, 686s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (4H, s, C2'*H*, C3'*H*, C5'*H*, C6'*H*), 7.63–7.66 (4H, m, C2*H*, C6*H*, C2''*H*, C6''*H*), 7.43–7.47 (4H, m, C3*H*, C5*H*, C3''*H*, C5''*H*), 7.32–7.39 (2H, m, C4*H*, C4''*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.7 (*C1*, *C1''*), 140.1 (*C1'*, *C4'*), 128.8 (*C3*, *C5*, *C3''*, *C5''*), 127.5 (*C2'*, *C3'*, *C5'*, *C6'*), 127.3 (*C4*, *C4''*), 127.0 (*C2*, *C6*, *C2''*, *C6''*); in agreement with literature data.[162]

4-Fluoro-3-(trifluoromethyl)-1,1'-biphenyl (5b):



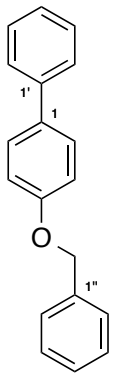
Prepared according to general procedure **A** using methyl 4-fluoro-3-(trifluoromethyl)-benzoate (22.2 mg, 100 µmol) and chromatography with pentane to give a colorless oil (19.1 mg, 80%): R_f 0.36 (pentane); ν_{max} (neat): 3037w, 2361m, 2352w, 1623w, 1513m, 1455w, 1414m, 1331s, 1273m, 1245s, 1164m, 1125s, 1055s, 900m, 862w, 833m, 758s, 721m, 696s, 664m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78–7.81 (1H, m, C2*H*), 7.71–7.75 (1H, m, C6*H*), 7.52–7.55 (2H, m, C2'*H*, C6'*H*), 7.44–7.48 (2H, m, C3'*H*, C5'*H*), 7.37–7.41 (1H, m, C4'*H*), 7.23–7.29 (1H, m, C5*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2 (d, $^1J_{CF}$ 256, *C4*), 138.9 (*C1'*), 137.7 (d, $^4J_{CF}$ 3.6, *C1*), 132.4 (d, $^3J_{CF}$ 9.1, *C6*), 129.1 (*C3'*, *C5'*), 128.1 (*C4'*), 127.1 (*C2'*, *C6'*), 125.8 (q, $^3J_{CF}$ 4.5, *C2*), 122.6 (q, $^1J_{CF}$ 265, *C*F_3), 118.6 (qd, $^2J_{CF}$ 33, 12, *C3*) 117.3 (d, $^2J_{CF}$ 21, *C5*). ^{19}F-NMR (376 MHz, $CDCl_3$): δ = –61.4 (3F, d, ^4J 12.9, C*F*$_3$), –117.4 (1F, q, ^4J 12.4, Ar*F*).

3-(Benzyloxy)-1,1'-biphenyl (5c):



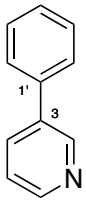
Prepared according to general procedure **A** using methyl 3-(benzyloxy) benzoate (24.2 mg, 100 µmol) and chromatography with pentane:CH_2Cl_2 9:1 to 85:15 to give a yellowish oil (15.3 mg, 59%): R_f 0.43 (pentane:CH_2Cl_2 8:2); ν_{max} (neat): 3062w, 3032w, 2924w, 2869w, 1596m, 1570m, 1477m, 1455w, 1421w, 1379w, 1296m, 1199s, 1052w, 1014m, 877w, 855w, 754s, 737s, 693s, 613w; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.59 (2H, m, C2'*H*, C6'*H*), 7.30–7.48 (9H, m, C5*H*, C3'*H*, C4'*H*, C5'*H*, C2''*H*–C6''*H*), 7.21–7.23 (1H, m, C2*H*), 7.18–7.21 (1H, m, C6*H*), 6.94–6.98 (1H, m, C4*H*), 5.12 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2 (*C3*), 142.8 (*C1*), 141.0 (*C1'*), 137.0 (*C1''*), 129.8, 128.7, 128.6, 128.0, 127.5, 127.4, 127.2 (*C2'*, *C6'*), 119.9 (*C6*), 113.9 (*C2*), 113.5 (*C4*), 70.1 (*C*H_2); in agreement with literature data.[163]

4-(Benzyloxy)-1,1'-biphenyl (5d):



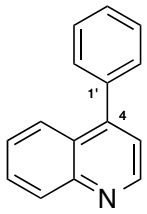
Prepared according to general procedure **A** with 300 µmol **1a** using methyl 4-(benzyloxy)benzoate (24.2 mg, 100 µmol) and chromatography with pentane:CH_2Cl_2 9:1 to 8:2 to give a beige solid (14.9 mg, 57%, m.p. 134.7–135.5 °C): R_f 0.29 (pentane:CH_2Cl_2 8:2); ν_{max} (neat): 3063w, 3035w, 2923w, 2867w, 2361w, 2341w, 1886w, 1744w, 1605m, 1583w, 1520m, 1467m, 1376m, 1284m, 1271m, 1245s, 1195s, 1176s, 1128m, 1022s, 1004s, 915m, 859m, 825s, 750s, 715s, 688s, 621s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53–7.56 (2H, m, C2'*H*, C6'*H*), 7.50–7.53 (2H, m, C3*H*, C5*H*), 7.44–7.47 (2H, m, C2''*H*, C6''*H*), 7.37–7.43 (4H, m, C2'*H*, C6'*H*, C3''*H*, C5''*H*), 7.31–7.35 (1H, m, C4''*H*), 7.28–7.31 (1H, m, C4'*H*), 7.03–7.07 (2H, m, C3*H*, C5*H*), 5.10 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.4 (*C4*), 140.8 (*C1*), 137.0 (*C1''*), 134.0 (*C1'*), 128.7, 128.6, 128.2 (*C3*, *C5*), 128.0 (*C4''*), 127.5 (*C2''*, *C6''*), 126.7 (*C2'*, *C6'*), 126.7 (*C4'*), 115.1 (*C2*, *C6*), 70.1 (*C*H_2); in agreement with literature data.[164]

3-Phenylpyridine (5e):



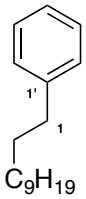
Prepared according to general procedure **A** using methyl nicotinate (13.7 mg, 100 µmol) and chromatography with pentane:Et_2O 1:1 to give a colorless oil (11.2 mg, 72%): R_f 0.20 (pentane:Et_2O 4:6); ν_{max} (neat): 3055w, 3031w, 2361m, 1582w, 1473m, 1451m, 1407s, 1336w, 1188w, 1076w, 1025w, 1006m, 914w, 813m, 753s, 696s, 639m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.86 (1H, dd, ^4J 2.4, ^5J 0.8, C2*H*), 8.59 (1H, dd, ^3J 4.8, C6*H*), 7.87 (1H, ddd, ^3J 7.9, ^4J 2.4, 1.7, C4*H*), 7.57–7.61 (2H, m, C2'*H*, C6'*H*), 7.46–7.51 (2H, m, C3'*H*, C5'*H*), 7.39–7.43 (1H, m, C4'*H*), 7.36 (1H, ddd, ^3J 7.9, 4.8, ^5J = 0.9, C5*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.5 (*C6*), 148.4 (*C2*), 137.9 (*C1'*), 136.7 (*C3*), 134.4 (*C4*), 129.1 (*C3'*, *C5'*), 128.1 (*C4'*), 127.2 (*C2'*, *C6'*), 123.6 (*C5*); ESI-MS: m/z calcd. for $C_{11}H_{10}N^+$ 156.0808 found 156.0808 [MH^+].

4-Phenylquinoline (5f):



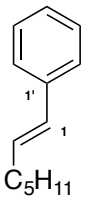
Prepared according to general procedure **A** using methyl quinoline-4-carboxylate (18.7 mg, 100 µmol) and chromatography with pentane:Et_2O 6:4 to give a yellowish gel (14.0 mg, 68%): R_f 0.20 (pentane:Et_2O 6:4); ν_{max} (neat): 3058w, 3032w, 2361s, 2340m, 1571m, 1491m, 1389m, 1277w, 1124w, 1075w, 1020w, 850s, 765s, 699s, 656m, 611s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.95 (1H, d, ^3J 4.4, C2*H*), 8.18 (1H, dd, ^3J 8.5, ^5J 0.6, C8*H*), 7.92 (1H, ddd, ^3J 8.5, ^4J 1.3, ^5J 0.5, C5*H*), 7.73 (1H, ddd, ^3J 8.8, 6.5, ^4J 1.4, C7*H*), 7.47–7.56 (6H, m, C6*H*, 5x Ph-*H*), 7.34 (1H, d, ^3J 4.4, C3*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.0 (*C2*), 148.7 (*C8a*), 148.5 (*C4*), 138.0 (*C1'*), 129.9 (*C8*), 129.5 (2x Ph*C*), 129.3 (*C7*), 128.6 (2x Ph*C*), 128.4 (*C4'*), 126.8 (*C4a*), 126.6 (*C6*), 125.9 (*C5*), 121.3 (*C3*); ESI-MS: m/z calcd. for $C_{15}H_{12}N^+$ 206.0964 found 206.0963 [MH^+].

Undecylbenzene (5g):



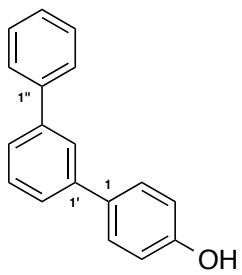
Prepared according to general procedure **A** using methyl laurate (21.4 mg, 100 µmol) and chromatography with pentane to give a colorless oil (15.8 mg, 68%): R_f 0.60 (pentane); ν_{max} (neat): 3736w, 3027w, 2923s, 2834s, 2361s, 2340m, 1496w, 1457m, 1377w, 1030w, 968w, 908w, 744m, 767s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25–7.29 (2H, m, C3'*H*, C5'*H*), 7.14–7.19 (3H, m, C2'*H*, C6'*H*, C4'*H*), 2.60 (2H, t, ^3J 7.8, C1*H*$_2$), 1.57–1.65 (2H, m, C2*H*$_2$), 1.22–1.35 (16H, m, C3*H*$_2$–C10*H*$_2$), 0.88 (3H, t, ^3J 7.0, C11*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.0 (*C1'*), 128.4 (*C2'*, *C6'*), 128.2 (*C3'*, *C5'*), 125.5 (*C4'*), 36.0 (*C1*), 31.9 (*C9*), 31.5 (*C2*), 29.7, 29.6, 29.5, 29.4, 22.7 (*C10*), 14.1 (*C11*); in agreement with literature data.[165]

(*E*)-Hept-1-en-1-ylbenzene (5h):



Prepared according to general procedure **A** using methyl (*E*)-oct-2-enoate (15.6 mg, 100 µmol) and chromatography with pentane to give a yellowish oil (10.4 mg, 60%): R_f 0.54 (pentane); ν_{max} (neat): 3735w, 3026w, 2957m, 2925s, 2856m, 2361s, 2340s, 1703w, 1598w, 1494m, 1452m, 1377w, 1071w, 1028w, 962s, 908w, 741s, 691s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 (2H, d, ^3J 7.6, C2'*H*, C6'*H*), 7.28 (2H, dd, ^3J 7.6, 7.6, C3'*H*, C5'*H*), 7.14–7.21 (1H, m, C4'*H*), 6.37 (1H, d, ^3J 15.9, C1*H*), 6.23 (1H, dt, ^3J 15.7, 6.9, C2*H*), 2.17–2.23 (2H, m, C3*H*$_2$), 1.43–1.50 (2H, m, C4*H*$_2$), 1.29–1.37 (4H, m, C5*H*$_2$, C6*H*$_2$), 0.90 (3H, t, ^3J 7.6, C7*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.0 (*C1'*), 131.3 (*C2*), 129.7 (*C1*), 128.5 (*C3'*, *C5'*), 126.7 (*C4'*), 125.9 (*C2'*, *C6'*), 33.0 (*C3*), 31.5 (*C5*), 29.1 (*C4*), 22.6 (*C6*), 14.1 (*C7);* in agreement with literature data.[166]

[1,1':3',1''-Terphenyl]-4-ol (5i):

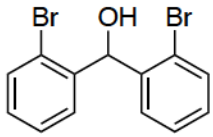


Prepared according to general procedure **A** with 300 µmol **1a** using methyl 4'-hydroxy-[1,1'-biphenyl]-3-carboxylate (22.8 mg, 100 µmol) and chromatography with pentane: CH_2Cl_2 25:75 to CH_2Cl_2 to give a yellowish solid (10.4 mg, 80%, m.p. 87.9–88.4 °C): R_f 0.30 (CH_2Cl_2); ν_{max} (neat): 3243m, 3030w, 2957w, 2361m, 2341w, 1597m, 1516s, 1475m, 1461m, 1439m, 1404m, 1376m, 1224s, 1182s, 1107m, 1017w, 899w, 832s, 790s, 756s, 725s, 696s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.73–

7.76 (1H, m, C2'*H*), 7.62–7.65 (2H, m, C2''*H*, C6''*H*), 7.50–7.55 (4H, m, C2*H*, C6*H*, C4'*H*, C6'*H*), 7.43–7.49 (3H, m, C5'*H*, C3''*H*, C5''*H*), 7.34–7.38 (1H, m, C4''*H*), 6.89–6.93 (2H, m, C3*H*, C5*H*), 4.94 (1H, s, O*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.2 (C4), 141.8 (C3'), 141.3 (C1''), 141.3 (C1'), 134.0 (C1), 129.2 (C5'), 128.8 (C3'', C5''), 128.5 (C2, C6), 127.4 (C4''), 127.3 (C2'', C6''), 125.7 (C2'), 125.7 (C4'), 125.6 (C6'), 115.7 (C3, C5); ESI-MS: m/z calcd. for $C_{18}H_{15}O^+$ 247.1117 found 247.1115 [MH^+].

Reagent preparation (Acenes)

Bis(2-bromophenyl)methanol (12):[109]



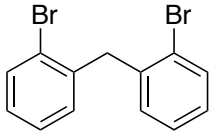
To a solution of isopropylmagnesium chloride lithium chloride complex in THF (100 mL, 1.30 molL^{-1}, 130 mmol) at –15 °C was added 1,2-dibromobenzene (14.9 mL, 0.124 mmol) over 30 min and the reaction mixture was stirred for 2 h at the same temperature. Ethyl formate (5.10 mL, 63.1 mmol) was added over 20 min at –15 °C and the reaction mixture was stirred for 1 h at the same temperature. An aqueous saturated solution of NH_4Cl (100 mL) and H_2O (70 mL) was added and the reaction mixture was allowed to warm to RT. The mixture was extracted with Et_2O (3 x 100 mL), the combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo*. Purification by chromatography (Et_2O:pentane 2:8 to 4:6) gave a white solid (16.9 g, 80%, m.p. 70.6–71.4 °C): R_f 0.29 (Et_2O:pentane 2:8); ν_{max} (neat): 3214m, 3063w, 2361w, 1731w, 1568w, 1465m, 1437m, 1329w, 1302w, 1270w, 1242w, 1183w, 1120w, 1016s, 945w, 869w, 818w, 747s, 726s, 682m, 641m; ^{1}H NMR (500 MHz, $CDCl_3$): [illegible] = 7.57 (2H, dd, ^3J 7.8, ^4J 1.0, C3*H*), 7.28–7.34 (4H, m, C5*H*, C6*H*), 7.18 (2H, ddd, ^3J 7.9, 6.9, ^4J 2.2, C4*H*), 6.40 (1H, d, ^3J 4.1, C*H*OH), 2.61 (1H, d, ^3J 4.2, O*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.9 (*C2*), 132.9 (*C3*), 129.4 (*C4*), 128.7 (*C6*), 127.6 (*C5*), 123.8 (*C1*) 74.2 (*C*HOH); ESI-MS: m/z calcd. for $C_{13}H_{10}Br_2NaO^+$ 362.8991 found 362.8992 [M+Na^+].

Alternative large scale procedure

To a solution of 1,2-dibromobenzene (56.8 mL, 471 mmol) in THF (100 mL)at –15 °C was added isopropylmagnesium chloride lithium chloride complex in THF (300 mL, 1.57 molL^{-1}, 471 mmol) over 1.5 h. The mixture was stirred at –15 °C for 1.5 h. At the same temperature, 2-bromobenzaldehyde (50.0 mL, 428 mmol) was added over 45 min and

the mixture was stirred at –15 °C for further 45 min. An aq sat. solution of NH_4Cl (100 mL) and H_2O (700 mL) was added and the reaction mixture was allowed to warm to RT. The mixture was diluted with Et_2O (600 mL), the phases were separated and the aq phase was extracted with Et_2O (2 x 300 mL), the combined organic phases were dried over Na_2SO_4 and the solvent was removed *in vacuo*. To the obtained yellow gel was added pentane (200 mL) and the suspension was stirred with a spatula and sonificated for 5 min. A white crystalline precipitate was formed, which was filtered off and washed with pentane (2 x 50 mL). Residual solvent was removed under reduced pressure. The pure product was obtained as a white solid (116 g, 80%, m.p. 79.8–81.3 °C).

Bis(2-bromophenyl)methane (13):



Dehydroxylation with HI in AcOH

Prepared according to a modified literature procedure.[112] To a solution of bis(2-bromophenyl)methanol (16.8 g, 49.1 mmol) in AcOH (330 mL) at RT was added HI (25.8 mL, 57% in H_2O, 196 mmol) and the reaction mixture was heated to reflux (130 °C) for 2 h. The reaction mixture was allowed to cool to RT over 14 h. An aqueous saturated solution of Na_2SO_3 (250 mL) was slowly added under vigorous stirring until no further color change from dark to yellow was observed. The mixture was diluted with H_2O (500 mL) and extracted with Et_2O (3 x 200 mL). The combined organic phases were cooled to 0°C and an aqueous solution of NaOH (50%, 400 mL) was slowly added until the washings were litmus blue. The aqueous phase was extracted with Et_2O (3 x 200 mL), the combined organic phases were washed with brine (100 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo*. Purification by chromatography (pentane) gave a light purple liquid (11.2 g, 70%): R_f 0.37 (pentane); ν_{max} (neat): 3058w, 3014w, 2907w, 1951w, 1920w, 1801w, 1693w, 1589w, 1566m, 1468m, 1438s, 1257w, 1185w, 1160w, 1115w, 1046m, 1024s, 946w, 913w, 854w, 802w, 742s, 660s, 616m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 (2H, dd, ^3J 8.0, ^4J 1.3, C3*H*), 7.22 (2H, ddd, ^3J 7.5, 7.5, ^4J 1.3, C5*H*), 7.11 (2H, ddd, ^3J 7.9, 7.4, ^4J 1.7, C4*H*), 6.98 (2H, dd, ^3J 7.6, ^4J 1.6, C6*H*), 4.20 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.9 (*C2*), 132.8 (*C3*), 130.7 (*C6*), 128.1 (*C4*), 127.5 (*C5*), 125.1 (*C1*), 42.1 (*C*H_2); in agreement with literature data.[109]

Dehydroxylation with NaI, TMSCl in MeCN (large scale)[110]

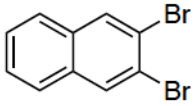
To a suspension of anhydrous sodium iodide (255 g, 1.70 mol) in MeCN (200 mL) at RT was added TMSCl (216 mL, 1.70 mmol) over 10 min. The suspension was stirred for 15 min at RT with a mechanical stirrer. A solution of bis(2-bromophenyl)methanol (116 g, 339 mmol) in MeCN (150 mL) was added over 15 min while maintaining the reaction at RT by cooling with an ice bath. Additional MeCN (200 mL) was added and the reaction mixture was stirred for 8 h at RT. An aqueous saturated solution of Na_2CO_3 (100 mL) and of Na_2SO_3 (150 mL) and H_2O (400 mL) was added and the MeCN was removed *in vacuo*. The residual mixture was extracted with Et_2O (4 x 300 mL). The combined organic phases were washed with brine (200 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo* to give a red oil. Red colored, presumably inorganic impurities were removed *in vacuo* (at 160 °C and 2.7 x 10^{-1} mbar) to give the pure desired product as a clear purple liquid (110 g, 99%).

1,5-Bifunctional Diarylmagnesium Reagent 15b (Anthracenes):

To a suspension of magnesium turnings (81.7 mg, 3.36 mmol, 2.40 eq.) in anhydrous THF (2.5 mL) at RT was added a solution of bis(2-bromophenyl)methane (456 mg, 1.40 mmol, 1.00 eq.) in anhydrous THF (2.5 mL). The mixture was repeatedly heated to mild reflux until a change in color was observed. The mixture was stirred at RT for 12 h. An aliquot was titrated in triplicates according to Eastham and Watson in order to determine the yield (92%) and the concentration (0.258 $molL^{-1}$ ±4.8%) of the reagent.[161] The reagent was used directly in the next step.

For scales > 350 µmol, the dibromides were added dropwise after a color change has been observed.

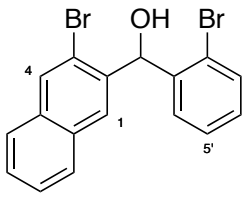
2,3-Dibromonaphthalene (25):



Prepared according to a modified literature procedure.[112] To a suspension of 1,2,4,5-tetrabromobenzene (7.87 g, 20.0 mmol) and furan (10.0 mL, 138 mmol) in dry toluene (200 mL) at –23 °C was added *n*-butyllithium in hexanes (200 mL, 0.110 $molL^{-1}$, 22.0 mmol) *via* a syringe pump over 3 h. The reaction mixture was allowed to warm to RT over 3.5 h. MeOH (1 mL) was added and the reaction mixture was washed with H_2O (2 x 40 mL). The aqueous phase was extracted with Et_2O (20 mL), the combined organic phases were dried over Na_2SO_4 and the solvent was

removed *in vacuo* to obtain a beige solid (6.00 g) of 6,7-dibromo-1,4-dihydro-1,4-epoxynaphthalene. To a suspension of Zn-dust (12.0 g, 184 mmol) in dry THF (300 mL) at 0 °C was slowly added $TiCl_4$ (12.0 mL, 109 mmol). The reaction mixture was heated to reflux for 5 min, cooled to 0 °C and a solution of 6,7-dibromo-1,4-dihydro-1,4-epoxynaphthalene (6.00 g, 20.0 mmol) in dry THF (120 mL) was added. The reaction mixture was heated to reflux for 22 h, cooled to 0 °C and ice-cold aqueous HCl (10%, 600 mL) was slowly added. The aqueous phase was extracted with CH_2Cl_2 (3 x 150 mL), the combined organic phases were washed with H_2O (200 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* to obtain a yellow solid (5.76 g), which was directly used for the following reactions. A small amount was purified by chromatography (pentane) to obtain white crystals (136.6–138.4 °C): R_f 0.45 (pentane); ν_{max} (neat): 3058m, 1964w, 1831w, 1712w, 1569m, 1483m, 1423m, 1307m, 1193m, 1146w, 1095m, 1040w, 945m, 886s, 752s, 634m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.14 (2H, s, C1*H*, C4*H*), 7.73 (2H, dd, ^3J 6.2, ^4J 3.2, C5*H*, C8*H*), 7.51 (2H, dd, ^3J 6.3, ^4J 3.2, C6*H*, C7*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 133.0 (*C4a*, *C8a*), 132.2 (*C1*, *C4*), 127.2 (*C6*, *C7*), 126.9 (*C5*, *C8*), 122.0 (*C2*, *C3*); in agreement with literature data.[109]

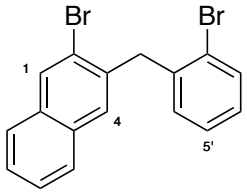
(3-Bromonaphthalen-2-yl)(2-bromophenyl)methanol (26):



Prepared according to a modified literature procedure.[109] To a solution of isopropylmagnesium chloride lithium chloride complex in THF (4.58 mL, 1.30 molL^{-1}, 5.95 mmol) at −15 °C was added a solution of 2,3-dibromonaphthalene (1.62 g, 5.67 mmol) in dry THF (10 mL) over 5 min and the reaction mixture was stirred for 2 h at the same temperature. 2-Bromobenzaldehyde (695 µL, 5.95 mmol) was added over 5 min at −15 °C and the reaction mixture was stirred for 30 min at the same temperature. An aqueous saturated solution of NH_4Cl (10 mL) and H_2O (5 mL) was added and the reaction mixture was allowed to warm to RT. The mixture was extracted with Et_2O (3 x 20 mL), the combined organic phases were dried over Na_2SO_4 and the solvent was removed *in vacuo*. Purification by chromatography (Et_2O: pentane 2:8) gave a white solid (1.59 g, 72%, m.p. 74.2–75.0 °C): R_f 0.23 (Et_2O:pentane 2:8); ν_{max} (neat): 3555w, 3267m, 3055w, 2920w, 2324w, 1626w, 1589w, 1569w, 1493w, 1466w, 1433m, 1323w, 1270w, 1237w, 1201w, 1159w, 1128w, 1049m, 1019s, 983s, 952w, 881m, 845w, 829w, 803w, 743s, 689m, 652w, 618w; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09

(1H, s, C4*H*), 7.84 (1H, s, C1*H*), 7.76–7.79 (1H, m, C8*H*), 7.73–7.76 (1H, m, C5*H*), 7.58–7.62 (1H, m, C3'*H*), 7.46–7.52 (2H, m, C6*H*, C7*H*), 7.27–7.30 (2H, m, C5'*H*, C6'*H*), 7.18–7.22 (1H, m, C4'*H*), 6.54 (1H, d, ^3J 3.8, C*H*OH), 2.69 (1H, d, ^3J 4.2, O*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.0 (*C2'*), 138.1(*C3*), 133.9 (*C4a*), 133.0 (*C3'*), 132.1 (*C8a*), 131.7 (*C4*), 129.5 (*C4'*), 128.8 (*C5'*), 128.2 (*C8*), 127.8 (*C9*), 127.7 (*C6'*), 127.1 (*C6*), 126.62 (*C5*), 126.58 (*C7*), 124.2 (*C1'*), 121.1 (*C2*), 74.3 (*CH*OH); ESI-MS: m/z calcd. for $C_{17}H_{12}Br_2NaO^+$ 412.9147 found 412.9146 [M+Na^+].

2-Bromo-3-(2-bromobenzyl)naphthalene (27):



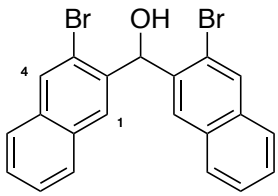
Prepared according to a modified literature procedure.[109] To a solution of (3-bromonaphthalen-2-yl)(2-bromophenyl)methanol (1.53 g, 3.90 mmol) in AcOH (40.0 mL) at RT was added HI (2.05 mL, 57% in H_2O, 15.6 mmol) and the reaction mixture was heated to reflux (130 °C) for 2 h. The reaction mixture was allowed to cool to RT over 14 h. An aqueous saturated solution of $Na_2S_2O_3$ (10 mL) was slowly added under vigorous stirring until no further color change from dark to yellow was observed. The mixture was diluted with H_2O (40 mL) and extracted with Et_2O (4 x 70 mL). The combined organic phases were cooled to 0 °C and an aqueous solution of NaOH (50%, 70 mL) was slowly added until the washings were litmus blue. The aqueous phase was extracted with Et_2O (20 mL), the combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was dissolved in CH_2Cl_2 and filtered through a plug of silica gel (CH_2Cl_2). The solvent was removed *in vacuo* and the residue was recrystallized from hot *n*-hexane (14 mL) to obtain white crystals (850 mg, 58%, m.p. 89.6–92.2 °C): R_f 0.28 (pentane); ν_{max} (neat): 3056w, 3031w, 2325w, 1786w, 1589w, 1563w, 1487w, 1462m, 1434m, 1329w, 1314w, 1269w, 1211w, 1130w, 1045w, 1027m, 986m, 954m, 884s, 806w, 745s, 692m, 653m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.13 (1H, s, C1*H*), 7.42–7.76 (1H, m, C8*H*), 7.65–7.69 (1H, m, C5*H*), 7.63 (1H, dd, ^3J 8.0, ^4J 1.3, C3'*H*), 7.42–7.48 (2H, m, C6*H*, C7*H*), 7.40 (1H, s, C4*H*), 7.22 (1H, ddd, ^3J 7.5, 7.5, ^4J 1.3, C5'*H*), 7.14 (1H, ddd, ^3J 7.8, 7.5, ^4J 1.7, C4'*H*), 7.01 (1H, dd, ^3J 7.6, ^4J 1.6, C6'*H*), 4.34 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.0 (*C2'*), 136.2 (*C2*), 133.3 (*C4a*), 132.9 (*C3'*), 132.4 (*C8a*), 131.4 (*C1*), 130.8 (*C6'*), 129.3 (*C4*), 128.1 (*C4'*), 127.5 (*C5*, *C5'*), 126.6 (*C8*), 126.5 (*C7*), 126.4

(*C6*), 125.1 (*C1'*), 123.2 (*C3*), 42.3 (CH_2); in agreement with literature data.[109]

1,5-Bifunctional Diarylmagnesium Reagent 30 (Tetracenes):

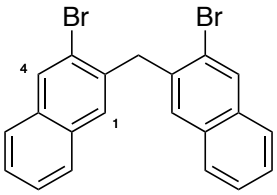
To a suspension of magnesium turnings (40.8 mg, 1.68 mmol, 2.40 eq.) in anhydrous THF (1.25 mL) at RT was added a solution of 2-bromo-3-(2-bromobenzyl)naphthalene (263 mg, 699 µmol, 1.00 eq.) in anhydrous THF (1.25 mL). The mixture was repeatedly heated to mild reflux until a change in color was observed. The mixture was stirred at RT for 12 h. An aliquot was titrated in triplicates according to Eastham and Watson in order to determine the yield (96%) and the concentration (0.273 $molL^{-1}$ ±1.3%) of the reagent.[161] The reagent was used directly in the next step.

Bis(3-bromonaphthalen-2-yl)methanol (28):[109]



To a solution of isopropylmagnesium chloride lithium chloride complex in THF (8.46 mL, 1.30 $molL^{-1}$, 11.0 mmol) at −15 °C was added a solution of 2,3-dibromonaphthalene (2.86 g, 10.0 mmol, see preparation of reagent **3c**) in dry THF (20 mL) over 5 min and the reaction mixture was stirred for 2 h at the same temperature. Ethyl formate (408 µL, 5.05 mmol) was added over 5 min at −15 °C and the reaction mixture was stirred for 1 h at the same temperature. An aqueous saturated solution of NH_4Cl (10 mL) and H_2O (5 mL) were added and the reaction mixture was allowed to warm to RT. The mixture was extracted with Et_2O (3 x 20 mL), the combined organic phases were dried over Na_2SO_4 and the solvent was removed *in vacuo*. Purification by chromatography (Et_2O:pentane 2:8 to 4:6) gave a white solid (1.49 g, 67%, m.p. 111.2–112.7 °C): R_f 0.21 (Et_2O:pentane 2:8); ν_{max} (neat): 3552w, 3246m, 3055w, 2922w, 2168w, 1724w, 1627w, 1589m, 1493m, 1430m, 1356w, 1326w, 1270m, 1202w, 1164w, 1127m, 1041s, 993m, 973s, 953m, 881s, 803m, 737s, 664w, 628w; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.13 (2H, s, C4*H*), 7.81 (2H, s, C1*H*), 7.74–7.79 (4*H*, m, C5*H*, C8*H*,), 7.47–7.54 (4H, m, C6*H*, C7*H*), 6.70 (1H, d, ^3J 4.4, C*H*OH), 2.74 (1H, d, ^3J 4.0, O*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.3, 133.9, 132.2, 131.8 (*C4*) 128.3, 128.0 (*C1*), 127.1, 126.7, 126.6, 121.4, 74.4 (*C*HOH); ESI-MS: m/z calcd. for $C_{21}H_{14}Br_2NaO^+$ 462.9304 found 462.9301 [$M+Na^+$].

Bis(3-bromonaphthalen-2-yl)methane (29):



Prepared according to a modified literature procedure.[109] To a solution of bis(3-bromonaphthalen-2-yl)methanol (1.49 g, 3.37 mmol) in AcOH (55.0 mL) at RT was added HI (1.77 mL, 57% in H_2O, 13.5 mmol) and the reaction mixture was heated to reflux (130 °C) for 2 h. The reaction mixture was allowed to cool to RT over 14 h. An aqueous saturated solution of Na_2SO_3 (50 mL) was slowly added under vigorous stirring until no further color change from dark to yellow was observed. The mixture was diluted with H_2O (50 mL) and extracted with Et_2O (3 x 70 mL). The combined organic phases were cooled to 0 °C and an aqueous solution of NaOH (50%, 70 mL) was slowly added until ≥ pH 12 was reached. The aqueous phase was extracted with Et_2O (50 mL), the combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was recrystallized from hot *n*-hexane: toluene 5:1 (60 mL) to give white crystals (810 mg, 56%, m.p. 156.2–157.3 °C): R_f 0.18 (pentane); ν_{max} (neat): 3055w, 2925w, 2360w, 1587m, 1491m, 1429m, 1415m, 1351m, 1271m, 1205m, 1131m, 1018w, 983s, 956m, 881s, 796w, 748s, 661w, 622w; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15 (2H, s, C4*H*), 7.76 (2H, dd, ^3J 8.0, ^4J 1.2, C5*H*), 7.65 (2H, dd, ^3J 7.9, ^4J 1.0, C8*H*), 7.41–7.48 (6H, m, C6*H*, C7*H*, C1*H*), 4.47 (2H, s, C2'*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.4 (*C3*), 133.3 (*C8a*), 132.4 (*C4a*), 131.5 (*C4*), 129.4 (*C1*), 127.6 (*C8*), 126.6 (*C5*), 126.5 (*C6*), 126.4 (*C7*), 123.3 (*C2*), 42.5 (*C2'*); in agreement with literature data.[109]

1,5-Bifunctional Diarylmagnesium Reagent 31 (Pentacenes):

To a suspension of magnesium turnings (20.4 mg, 840 µmol, 2.40 eq.) in anhydrous THF (0.625 mL) at RT was added a solution of bis(3-bromonaphthalen-2-yl)methane (149.2 mg, 350 µmol, 1.00 eq.) in anhydrous THF (0.625 mL). The mixture was repeatedly heated to mild reflux until a change in color was observed. The mixture was stirred at RT for 12 h. An aliquot was titrated in triplicates according to Eastham and Watson in order to determine the yield (89%) and the concentration (0.248 molL^{-1} ±1.8%) of the reagent.[161] The reagent was used directly in the next step.

Ester to Acene Transformation

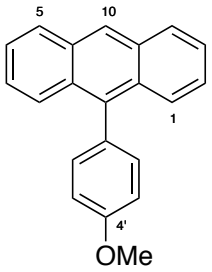
General Procedure B for Anthracenes and Tetracenes:

A solution of carboxylic acid ester (100 µmol) in anhydrous THF (1.00 mL) at RT was treated with reagent **15b** or **30** in THF (140 µmol) and stirred at RT for 4 h. Aqueous HCl (1.00 mL, 1.00 molL^{-1}) was added and the mixture was extracted with Et_2O (6 x 1.0 mL). The organic layers were washed with brine (1.0 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by chromatography (eluent specified below) to yield the corresponding anthracene and tetracene products.

Reactions to **16g** and **16h** were performed with 200 µmol and 240 µmol of reagent **15b**, respectively.

Tetracene derivatives **32a** and **32b** decomposed partially when dissolved in non-degased $CDCl_3$ or acetonitrile. Extractions could be performed in the dark. NMR samples were stable in solution for at least 12 h when measured in a brown glass tube with degased $CDCl_3$. Undissolved, dry tetracene derivatives **32a** and **32b** stored in the dark at RT remained stable for at least 30 days.

9-(4-Methoxyphenyl)anthracene (16a):



Prepared according to general procedure **B** using methyl 4-methoxybenzoate (16.6 mg, 100 µmol), reagent **15b** (543 µL, 0.258 molL^{-1}, 140 µmol), chromatography with pentane:CH_2Cl_2 80:20 to 50:50 to 30:70 to give a yellowish white solid (27.6 mg, 97%, m.p. 168.5–170.1 °C): R_f 0.49 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3037w, 2997w, 2962w, 2931w, 2907w, 2836w, 2048w, 1899w, 1604w, 1509m, 1441m, 1412w, 1358m, 1284m, 1239s, 1174s, 1105m, 1028s, 933w, 887m, 850m, 821s, 793m, 776m, 740s, 655m, 611s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.46 (1H, s, C10*H*), 8.02 (2H, ddd, ^3J 8.5, ^4J 0.6, 0.6, C4*H*, C5*H*), 7.71 (2H, dd, ^3J 8.8, ^4J 1.0, C1*H*, C8*H*), 7.43 (2H, ddd, ^3J 8.5, 6.5, ^4J 1.2, C3*H*, C6*H*), 7.30–7.37 (4H, m, C2*H*, C7*H*, C2'*H*, C6'*H*), 7.08–7.13 (2H, m, C3'*H*, C5'*H*), 3.93 (3H, s, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.0 (*C4'*), 136.8 (*C9*), 132.3 (*C2'*, *C6'*), 131.4 (*C4a*, *C10a*), 130.8 (*C1'*), 130.5 (*C8a*, *C9a*), 128.3 (*C4*, *C5*), 126.9 (*C1*, *C8*), 126.4 (*C10*), 125.2 (*C2*, *C7*), 125.0 (*C3*, *C6*), 113.8 (*C3'*, *C5'*), 55.4 (*C*H$_3$); ESI-MS: m/z calcd. for $C_{21}H_{16}O^{\cdot+}$ 284.1196 found 284.1194 [$M^{\cdot+}$].

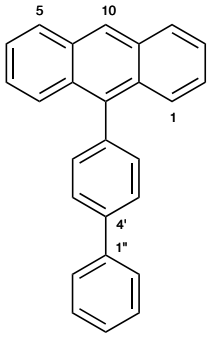
1.00 mmol scale:

Prepared according to general procedure **B** using methyl 4-methoxybenzoate (166 mg, 1.00 mmol), reagent **15b** (0.737 µL, 0.190 molL^{-1}, 140 µmol), chromatography with entane:CH_2Cl_2 80:20 to 50:50 to 30:70 to give a yellowish white solid (281 mg, 99%).

10.0 mmol scale:

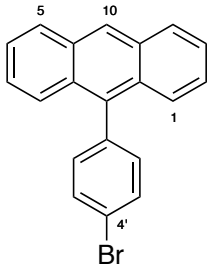
Prepared according to general procedure **B** using methyl 4-methoxybenzoate (1.66 g, 10.0 mmol), reagent **15b** (667 µL, 0.210 molL^{-1}, 140 µmol), chromatography with pentane:CH_2Cl_2 80:20 to 50:50 to 30:70 to give a yellowish white solid (2.67 g, 94%).

9-([1,1'-Biphenyl]-4-yl)anthracene (16c):



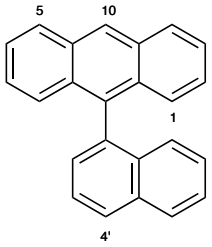
Prepared according to general procedure **B** using methyl biphenyl-4-carboxylate (21.2 mg, 100 µmol), reagent **15b** (560 µL, 0.250 molL^{-1}, 140 µmol), chromatography with pentane 100% to pentane: Et_2O, 80:5 to give a light yellow solid (32.7 mg, 99%, m.p. 212.2–213.1 °C): R_f 0.66 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3057w, 3027w, 1917w, 1803w, 1598w, 1518w, 1488w, 1479w, 1439m, 1413w, 1360m, 1178w, 1105w, 1075w, 1036w, 1006m, 934w, 908w, 891m, 860w, 847m, 824m, 792w, 758s, 731s, 693s, 653m, 611m, 581w, 554m, 541w, 499m, 433w, 418m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.51(1H, s, C10*H*), 8.05 (2H, ddd, ^3J 8.5, ^4J 0.6, 0.6, C4*H*, C5*H*), 7.81 (2H, m, C2'*H*, C6'*H*) 7.76 (4H, m, C1*H*, C8*H*, C2"*H*, C6"*H*), 7.51 (4H, m, C3'*H*, C5'*H*, C3"*H*, C5"*H*), 7.46 (2H, ddd, ^3J 8.4, 6.5, ^4J 1.1, C3*H*, C6*H*), 7.40 (1H, m, C4"*H*), 7.36 (2H, ddd, ^3J 8.3, 6.5, ^4J 1.3, C2*H*, C7*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.9 (*C1"*), 140.2 (*C4'*), 137.8 (*C9*), 136.7 (*C1'*), 131.7 (*C3'*, *C5'*), 131.4 (*C4a*, *C10a*), 130.2 (*C8a*, *C9a*), 128.9 (*C3"*, *C5"*), 128.4 (*C5*, *C4*), 127.4 (*C4"*), 127.2 (*C2"*, *C6"*), 127.0 (*C2'*, *C6'*), 126.8 (*C1*, *C8*), 126.6 (*C10*), 125.4 (*C2*, *C7*), 125.1 (*C3*, *C6*); ESI-MS: m/z calcd. for $C_{26}H_{18}^{\cdot+}$ 330.1403 found 330.1400 [$M^{\cdot+}$].

9-(4-Bromophenyl)anthracene (16d):



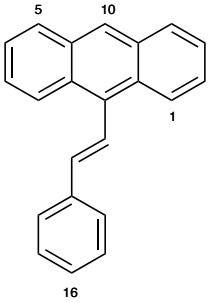
Prepared according to general procedure **B** using methyl 4-bromobenzoate (21.5 mg, 100 µmol), reagent **15b** (576 µL, 0.243 molL^{-1}, 140 µmol), chromatography with pentane 100% to pentane:CH_2Cl_2 2:1 to give a beige solid (32.9 mg, 99%, m.p. 173.7–175.9 °C): R_f 0.77 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3051w, 2921w, 2861w, 2325w, 1923w, 1799w, 1622w, 1585w, 1476m, 1442m, 1410m, 1386m, 1358m, 1261w, 1187w, 1166m, 1093w, 1066m, 1009s, 930m, 888s, 848m, 810s, 787m, 810s, 787m, 736s, 705s, 645m, 609s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.50 (1H, s, C10*H*), 8.04 (2H, ddd, ^3J 8.5, ^4J 0.5, 0.5, C4*H*, C5*H*), 7.69–7.73 (2H, m, C3'*H*, C5'*H*), 7.62 (2H, dd, ^3J 8.8, ^4J 0.9, C1*H*, C8*H*), 7.46 (ddd, ^3J 8.5, 6.5, ^4J 1.3, C3*H*, C6*H*), 7.36 (2H, ddd, ^3J 8.8, 6.5, ^4J 1.3, C2*H*, C7*H*), 7.28–7.33 (2H, m, C2'*H*, C6'*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.7 (*C4'*), 135.4 (*C9*), 133.0 (*C2'*, *C6'*), 131.6 (*C3'*, *C5'*), 131.3 (*C4a*, *C10a*), 130.0 (*C8a*, *C9a*), 128.4 (*C4*, *C5*), 127.0 (*C10*), 126.4 (*C1*, *C8*), 125.6 (*C2*, *C7*), 125.2 (*C3*, *C6*), 121.7 (*C1'*); ESI-MS: m/z calcd. for $C_{20}H_{13}Br^{\cdot+}$ 332.0195 found 332.0192 [$M^{\cdot+}$].

9-(Naphthalen-1-yl)anthracene (16e):



Prepared according to general procedure **B** using methyl 1-naphthoate (18.6 mg, 100 µmol), reagent **15b** (576 µL, 0.243 molL^{-1}, 140 µmol), chromatography with pentane 100% to pentane:CH_2Cl_2 20:1 to give a beige solid (29.4 mg, 97%, decomp. at 152.6 °C): R_f 0.69 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3050w, 2360w, 1931w, 1623w, 1590w, 1503m, 1443m, 1392w, 1349m, 1312w, 1257m, 1218w, 1143w, 1103w, 1074w, 1013m, 975w, 957w, 925m, 890m, 847m, 798s, 778s, 735s, 621m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.58 (1H, s, C10*H*), 8.09 (2H, d, ^3J 8.6, C4*H*, C5*H*), 8.04 (1H, d, ^3J 8.3, C4'*H*), 7.99 (1H, d, ^3J 8.3, C5'*H*), 7.68 (1H, dd, ^3J 8.3, 6.9, C3'*H*), 7.52 (1H, dd, ^3J 7.0, ^4J 1.2, C2'*H*), 7.45 (3H, m, C3*H*, C6*H*, C6'*H*), 7.39 (2H, dd, ^3J 8.9, ^4J 0.9, C1*H*, C8*H*), 7.23 (2H, ddd, ^3J 8.9, 6.5, ^4J 1.2, C2*H*, C7*H*), 7.18 (1H, ddd, ^3J 8.9, 6.9, ^4J 1.3, C7'*H*), 7.06 (1H, dd, ^3J 8.4, ^4J 0.7, C8'*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.5 (*C1'*), 134.9 (*C9*), 133.7 (*C4a'*), 133.5 (*C8a'*), 131.4 (*C4a*, *C10a*), 131.0 (*C8a*, *C9a*), 129.1 (*C2'*), 128.4 (*C4*, *C5*), 128.2 (*C4'*), 128.1 (*C5'*), 126.9 (*C1*, *C8*), 126.9 (*C10*), 126.5 (*C8'*), 126.2 (*C7'*), 125.9 (*C6'*), 125.5 (*C3'*), 125.5 (*C2*, *C7*), 125.2 (*C3*, *C6*); ESI-MS: m/z calcd. for $C_{24}H_{16}^{\cdot+}$ 304.1247 found 304.1247 [$M^{\cdot+}$].

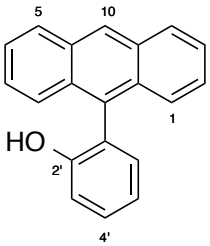
(*E*)-9-Styrylanthracene (16f):



Prepared according to general procedure **B** using methyl cinnamate (16.2 mg, 100 µmol), reagent **15b** (600 µL, 0.233 molL^{-1}, 140 µmol), chromatography with pentane:CH_2Cl_2 50:1 to 20:1 to 10:1 to 5:1 to 2:1 to give a yellow solid (24.3 mg, 87%, m.p. 129.5–130.6 °C): R_f 0.68 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3010w, 2326w, 1922w, 1799w, 1709w, 1621w, 1493m, 1448m, 1409w, 1352m, 1254w, 1203w, 1151w, 1075m, 1020m, 965s, 878s, 851m, 781m, 735s, 688s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.41 (1H, s, C10*H*), 8.36 (2H, m, C1*H*, C8*H*), 8.02 (2H, m, C4*H*, C5*H*), 7.92 (1H, dd, ^3J 16.6, ^4J 0.5, C12*H*), 7.68 (2H, m, C14*H*, C18*H*), 7.46 (6H, m, C2*H*, C3*H*, C6*H*, C7*H*, C15*H*, C17*H*), 7.36 (1H, m, C16*H*), 6.96 (d, ^3J 16.6, C11*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.3 (*C11*, *C13*), 132.8 (*C9*), 131.5 (*C4a*, *C10a*), 129.7 (*C8a*, *C9a*), 128.8 (*C15*, *C17*), 128.7 (*C4*, *C5*), 128.0 (*C16*), 126.6 (*C14*, *C18*), 126.5 (*C10*), 126.0 (*C1*, *C8*), 125.5 (*C2*, *C7*), 125.2 (*C3*, *C6*), 124.9 (*C12*); ESI-MS: m/z calcd. for $C_{22}H_{16}^{\cdot+}$ 280.1247 found 280.1243 [$M^{\cdot+}$].

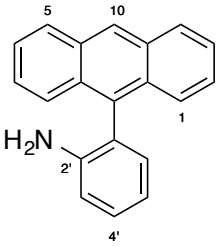
Partial decomposition of (*E*)-9-styrylanthracene **6n** at RT in clear glass container observed within two month.

2-(Anthracen-9-yl)phenol (16g):



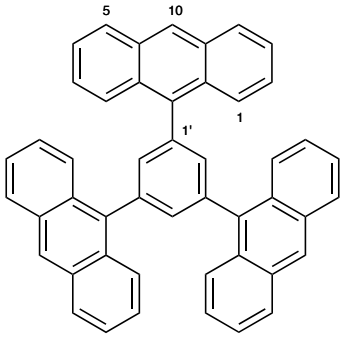
Prepared according to general procedure **B** using methyl salicylate (15.2 mg, 100 µmol), reagent **15b** (823 µL, 0.243 molL^{-1}, 200 µmol), chromatography with pentane:CH_2Cl_2 10:1 to 5:1 to 3:2 to 1:1 to give a yellowish beige solid (23.7 mg, 88%, decomp. at 181.8 °C): R_f 0.24 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3467s, 3027w, 1614w, 1579w, 1568w, 1518w, 1489m, 1478m, 1458m, 1440m, 1410w, 1358w, 1338w, 1283m, 1263m, 1242w, 1202w, 1174s, 1157s, 1141m, 1094m, 1030m, 1013m, 960w, 896m, 889m, 844m, 802m, 790m, 750s, 735s, 684m, 640m, 611m, 558m, 539s, 528m, 468m, 434m, 413s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.56 (1H, s, C10*H*), 8.07 (2H, ddd, ^3J 8.5, ^4J 0.6, 0.6, C4*H,* C5*H*), 7.67 (2H, ddd, ^3J 8.8, ^4J 1.9, ^5J 0.9, C1*H*, C8*H*), 7.49 (3H, m, C3*H*, C6*H*, C3'*H*), 7.41 (2H, ddd ^3J 8.8, 6.5, ^4J 1.3, C2*H*, C7*H*), 7.26 (1H, dd, ^3J 7.5, ^4J 1.6, C6'*H*), 7.15 (2H, m, C4'H, C5'*H*), 4.50 (1H, s, O*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.8 (*C2'*) 132.2 (*C6'*), 131.6 (*C4a, C10a*), 130.8 (*C8a, C9a*), 129.9 (*C3'*), 129.6 (*C9*), 128.6 (*C4, C5*) 128.0 (*C10*), 126.4 (*C2, C7*), 126.0 (*C1, C8*), 125.5 (*C3, C6*), 124.0 (*C1'*), 120.7 (*C5'*), 115.7 (*C4'*); ESI-MS: m/z calcd. for $C_{20}H_{14}NaO^+$ 293.0937 found 293.0934 [$M+Na^+$].

2-(Anthracen-9-yl)aniline (16h):



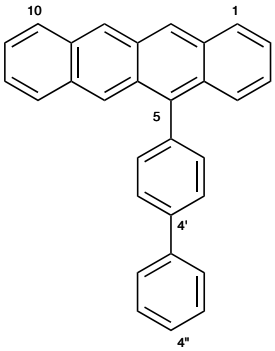
Prepared according to general procedure **B** using methyl 2-aminobenzoate (15.1 mg, 100 µmol), reagent **15b** (1.20 mL, 0.233 molL^{-1}, 240 µmol), additional extraction with CH_2Cl_2 (6 x 1.0 mL) and chromatography with pentane 100% to pentane:CH_2Cl_2 20:1 to 10:1 to 5:1 to give a brown solid (26.6 mg, 99%, m.p. 126.9–127.9 °C): R_f 0.11 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3474w, 3383m, 3048w, 3024w, 2360w, 1922w, 1807w, 1608s, 1497m, 1451s, 1356w, 1296m, 1257w, 1224w, 1186w, 1158w, 1031w, 1012w, 935m, 890m, 880m, 844m, 790m, 731s, 638m, 611m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.51 (1H, s, C10*H*), 8.05 (2H, d, ^3J 8.5, C4*H*, C5*H*), 7.70 (2H, dd, ^3J 8.8, ^4J 0.8, C1*H*, C8*H*), 7.47 (2H, ddd, ^3J 8.8, 6.6, ^4J 1.2, C3*H*, C6*H*), 7.38 (2H, ddd, ^3J 8.7, 6.5, ^4J 1.3, C2*H*, C7*H*), 7.34–7.38 (1H, m, C4'*H*), 7.16 (1H, dd, ^3J 7.5, ^4J 1.5, C6'*H*), 6.96 (1H, ddd, ^3J 8.0, 7.4, ^4J 1.2, C5'*H*), 6.93 (1H, dd, ^3J 8.1, ^4J 0.9, C3'*H*), 3.31 (2H, s, N*H*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.0 (*C2'*), 133.2 (*C9*), 132.1 (*C6'*), 131.7 (*C4a*, *C10a*), 130.3 (*C8a*, *C9a*), 129.0 (*C4'*), 128.5 (*C4*, *C5*), 127.0 (*C10*), 126.4 (*C1*, *C8*), 125.8 (*C2*, *C7*), 125.3 (*C3*, *C6*), 123.5 (*C1'*), 118.5 (*C5'*), 115.5 (*C3'*); ESI-MS: m/z calcd. for $C_{20}H_{16}N^+$ 270.1277 found 270.1279 [M+H$^+$].

1,3,5-Tri(anthracen-9-yl)benzene (16i):



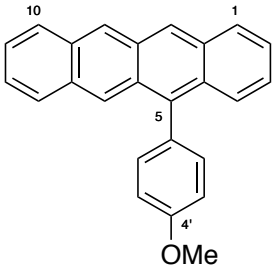
Prepared according to general procedure **B** using trimethyl 1,3,5-benzenetricarboxylate (25.2 mg, 100 µmol), reagent **15b** (2.20 mL, 0.192 molL^{-1}, 420 µmol), additional treatment with concentrated aqueous HCl (32%, five drops), chromatography with pentane 100% to pentane:CH_2Cl_2 20:1 to give a yellow solid (33.3 mg, 55%, decomp. at 296.6 °C): R_f 0.53 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3054m, 1941w, 1798w, 1690w, 1589m, 1519w, 1443m, 1402m, 1343m, 1260w, 1221w, 1164w, 1136w, 1014m, 953m, 887s, 865m, 843s, 787s, 731s, 652w, 612s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.48 (3H, s, C10*H*), 8.18 (6H, dd, ^3J 8.7, ^4J 1.0, C1*H*, C8*H*), 8.03 (6H, ddd, ^3J 8.4, ^4J 0.7, 0.7, C4*H*, C5*H*), 7.75 (3H, s, C2'*H*), 7.53 (6H, ddd, ^3J 8.4, 6.8, ^4J 1.4, C2*H*, C7*H*), 7.48 (6H, ddd, ^3J 8.5, 6.8, ^4J 1.3, C3*H*, C6*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.9 (*C9*), 136.2 (*C1'*), 133.7 (*C2'*), 131.4 (*C4a*, *C10a*), 130.3 (*C8a*, *C9a*), 128.5 (*C4*, *C5*), 126.9 (*C10*), 126.6 (*C1*, *C8*), 125.7 (*C2*, *C7*), 125.1 (*C3*, *C6*); in agreement with literature data.[167]

5-([1,1'-Biphenyl]-4-yl)tetracene (32a):



Prepared according to general procedure **B** using methyl biphenyl-4 carboxylate (21.2 mg, 100 µmol), reagent **30** (460 µL, 0.305 molL^{-1}, 140 µmol), chromatography with pentane 100% to pentane:CH_2Cl_2 100:1 to 20:1 to give an orange solid (23.2 mg, 61%, decomp. at 206.3 °C): R_f 0.67 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3050w, 3029w, 1921w, 1803w, 1691w, 1598w, 1485m, 1464w, 1448w, 1414w, 1391m, 1355w, 1323w, 1308w, 1285w, 1197w, 1161w, 1122w, 1112w, 1077w, 1006m, 959w, 947w, 895s, 837m, 785w, 744s, 728s, 698s, 667w, 651w; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.72 (1H, s, C11*H*), 8.69 (1H, s, C12*H*), 8.36 (1H, s, C6*H*), 8.03 (1H, d, ^3J 8.6, C10*H*), 7.98 (1H, d, ^3J 8.6, C1*H*), 7.86 (2H, m, C3'*H*, C5'*H*), 7.82 (1H, d, ^3J 8.6, C7*H*), 7.80 (2H, m, C2"*H*, C6"*H*), 7.73 (1H, d, ^3J 8.9, C4*H*), 7.57 (2H, m, C2'*H*, C6'*H*), 7.53 (2H, m, C3"*H*, C5"*H*), 7.42 (1H, m, C4"*H*), 7.37 (2H, m, C2*H*, C9*H*), 7.30 (2H, m, C3*H*, C8*H*); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 140.8 (*C1"*), 140.3 (*C4'*), 138.0 (*C1'*), 136.5 (*C5*), 131.9 (*C2'*, *C6'*), 131.4 (*C4a*), 131.2 (*C10a*, *C12a*), 130.0 (*C11a*), 129.7 (*C6a*), 129.4 (*C5a*), 128.9 (*C3"*, *C5"*), 128.8 (*C7*), 128.5 (*C10*), 127.9 (*C1*), 127.5 (*C4'*), 127.2 (*C2"*, *C6"*), 127.1 (*C3'*, *C5'*), 126.8 (*C4*), 126.8 (*C11*), 126.4 (*C12*), 125.6 (*C6*), 125.3 (*C9*), 125.2 (*C8*), 125.0 (*C3*), 124.8 (*C2*); ESI-MS: m/z calcd. for $C_{30}H_{20}^{\cdot+}$ 380.1560 found 380.1558 [$M^{\cdot+}$].

5-(4-Methoxyphenyl)tetracene (32b):



Prepared according to general procedure **B** using methyl 4-methoxybenzoate (16.6 mg, 100 µmol), reagent **30** (460 µL, 0.305 molL^{-1}, 140 µmol), chromatography with pentane 100% to pentane:CH_2Cl_2 100:1 to 2:1 to give a yellow solid (29.7 mg, 89%, decomp. at 203.4 °C): R_f 0.47 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3037w, 3001w, 2958w, 2928w, 2903w, 2834w, 1607m, 1511m, 1459w, 1439m, 1412w, 1394w, 1356w, 1324w, 1303w, 1284m, 1244s, 1173m, 1102m, 1026s, 960w, 949w, 896s, 824s, 798s, 746s, 704w. 663w; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.71 (1H, s, C11*H*), 8.69 (1H, s, C12*H*), 8.33 (1H, s, C6*H*), 8.02 (1H, d, ^3J 8.6, C10*H*), 7.99 (1H, d, ^3J 8.5, C1*H*), 7.82 (1H, d, ^3J 8.6, C7*H*), 7.70 (1H, d, ^3J 9.0, C4*H*), 7.43 (2H, m, C2'*H*, C6'*H*), 7.38 (2H, m, C2*H*, C9*H*), 7.32 (1H, m, C8*H*), 7.27

(1H, ddd, ^{3}J 8.9, 6.4, ^{4}J 1.1, C3*H*), 7.18 (2H, m, C3'*H*, C5'*H*), 3.99 (3H, s, C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.1 (*C4'*), 136.7 (*C5*), 132.5 (*C2'*, *C6'*), 131.3 (*C4a*), 131.2 (*C12a*), 131.1 (*C10a*), 131.0 (*C1'*), 130.0 (*C11a*), 129.9 (*C6a*), 129.7 (*C5a*), 128.8 (*C7*), 128.5 (*C10*), 127.9 (*C1*), 126.9 (*C4*), 126.5 (*C11*), 126.4 (*C12*), 125.7 (*C6*), 125.3 (*C9*), 125.0 (*C3*), 124.9 (*C8*), 124.8 (*C2*), 113.9 (*C3'*, *C5'*), 55.4 (*C*H$_3$); ESI-MS: m/z calcd. for $C_{25}H_{18}O^{\cdot+}$ 334.1352 found 334.1351 [$M^{\cdot+}$].

General Procedure C for Pentacenes 33a and 33b:

A solution of the specified carboxylic acid ester (100 µmol) in anhydrous THF (1.00 mL) at RT was treated with reagent **31** in THF (140 µmol) and stirred at RT for 4 h. Aqueous HCl (1.00 mL, 1.00 molL^{-1}) was added and the mixture was extracted with Et_2O (6 x 1.0 mL). The solvent was removed *in vacuo* and the residue was purified by washing the resulting solid (solvent specified below) under inert conditions (see below) to yield products **33a** and **33b**.

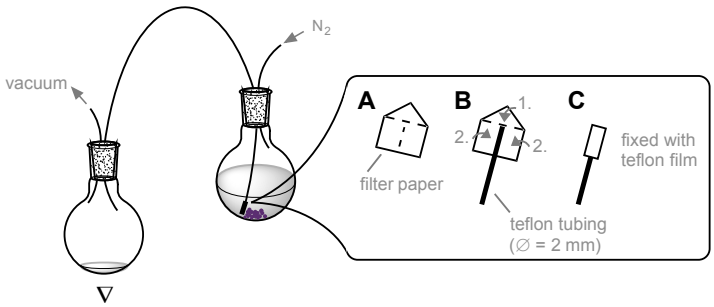
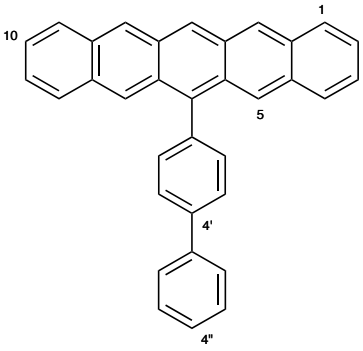


Figure **18**: Procedure to wash pentacene derivatives **33a** and **33b** under inert conditions: A) cut filter paper, B) fold around Teflon tubing, C) fix filter paper with teflon film on tubing.

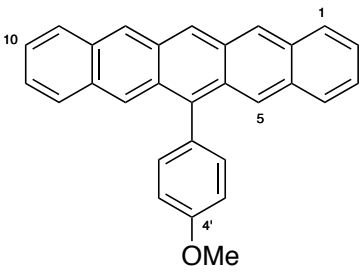
Pentacene derivatives **33a** and **33b** decomposed within 30 minutes in non-degased $CDCl_3$ or acetonitrile. Extractions could be performed in the dark. NMR samples were stable in solution for at least 12 h when measured in brown glass tube and with degased $CDCl_3$. Undissolved, dry pentacene derivatives **33a** and **33b** stored in the dark at RT remained stable for at least 30 days.

6-([1,1'-Biphenyl]-4-yl)pentacene (33a):



Prepared according to general procedure **C** using methyl biphenyl-4 carboxylate (21.2 mg, 100 µmol), reagent **31** (565 µL, 0.248 molL^{-1}, 140 µmol), washing the crude residue with H_2O (3 x 5 mL), EtOH (4 x 5 mL), dissolved in CH_2Cl_2 at 0 °C and removal of solvents *in vacuo* to give a black-blue solid (41.7 mg, 96.9 µmol, 97%, decomp. at 230.4 °C): R_f 0.58 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3660w, 2971w, 2914w, 2342w, 2153w, 1666w, 1486m, 1379w, 1262w, 1192w, 1158w, 1107m, 1008m, 960w, 901s, 836m, 805w, 768m, 733s, 697s, 647w; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.05 (1H, s, C13*H*), 8.72 (2H, s, C12*H*, C14*H*), 8.38 (2H, s, C5*H*, C7*H*), 7.94 (4H, m, C1*H*, C11*H,* C3'*H*, C5'*H*), 7.87 (2H, d, ^3J 3.8, C2"*H*, C6"*H*), 7.78 (2H, d, ^3J 8.6, C4*H*, C8*H*), 7.67 (2H, d, ^3J 8.0, C2'*H*, C6'*H*), 7.57 (2H, dd, ^3J 7.7, 7.7, C3"*H*, C5"H), 7.45 (1H, dd, ^3J 7.4, 7.4, C4"*H*), 7.32 (2H, dd, ^3J 7.4, 7.4, C2*H*, C10*H*), 7.26 (2H, dd, ^3J 7.4, 7.4, C3*H*, C9*H*); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 139.8 (*C1"*), 139.3 (*C4'*), 137.2 (*C1'*), 135.4 (*C6*), 131.1 (*C2'*, *C6'*), 130.5 (*C4a*, *C7a*) 130.2 (*C11a*, *C14a*), 128.9 (*C12a*, *C13a*), 128.0 (*C3"*, *C5"*), 127.9 (*C5a*, *C6a*), 127.9 (*C4*, *C8*), 127.0 (*C1*, *C11*), 126.5 (*C4"*), 126.2 (*C3'*, *C5'*), 126.2 (*C2"*, *C6"*) 125.8 (*C13*), 125.4 (*C12*, *C14*), 124.4 (*C5*, *C7*), 124.3 (*C2*, *C10*), 124.0 (*C3*, *C9*); ESI-MS: m/z calcd. for $C_{34}H_{22}^{\cdot+}$ 430.1716 found 430.1714 [$M^{\cdot+}$].

6-(4-Methoxyphenyl)pentacene (33b):



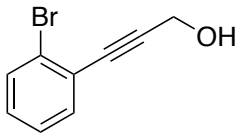
Prepared according to general procedure **C** using methyl 4-methoxybenzoate (16.6 mg, 100 µmol), reagent **31** (565 µL, 0.248 molL^{-1}, 140 µmol), washing the crude residue with hexanes (5 x 5 mL), H_2O (3 x 5 mL), MeOH (4 x 5 mL), dissolved in CH_2Cl_2 at RT and removal of solvents *in vacuo* to give a black-blue solid (31.5 mg, 82%, decomp. at 198.7 °C): R_f 0.42 (pentane:CH_2Cl_2 2:1); ν_{max} (neat): 3034w, 2929w, 2832w, 1667w, 1607m, 1505m, 1460w, 1436w, 1379w, 1343w, 1282m, 1244s, 1173m, 1105m, 1029m, 960m, 902s, 881m, 871m, 849w, 826m, 802w, 727s, 574m, 559m, 464s, 421w; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.98 (1H, s, C13*H*), 8.66 (2H, s,

C12*H*, C14*H*), 8,33 (2H, s, C5*H*, C7*H*), 7.91 (2H, d, ^{3}J 8.6, C1*H*, C11*H*), 7.75 (2H, d, ^{3}J 8.6, C4*H*, C8*H*), 7.49 (2H, d, ^{3}J 8.3, C2'*H*, C6'*H*), 7.30 (2H, dd, ^{3}J 7.3, C2*H*, C10*H*), 7.24 (4H, m, C3*H*, C9*H*, C3'*H*, C5'*H*), 4.03 (3H, s, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.2 (*C4'*), 136.6 (*C6*), 132.7 (*C2'*, *C6'*), 131.4 (*C4a*, *C7a*), 131.3 (*C1'*), 131.2 (*C11a*, *C14a*), 129.9 (*C12a*, *C13a*), 129.2 (*C5a*, *C6a*), 128.9 (*C4*, *C8*), 128.0 (*C1*, *C11*), 126.6 (*C13*), 126.4 (*C12*, *C14*), 125.6 (*C5*, *C7*), 125.2 (*C2*, *C10*), 124.9 (*C3*, *C9*), 114.0 (*C3'*, *C5'*), 55.4 (*C*H_3); ESI-MS: m/z calcd. for $C_{29}H_{20}O^{\cdot+}$ 384.1509 found 384.1510 [$M^{\cdot+}$].

Studies on the Ester to Naphthalene and Phenanthrene Transformation

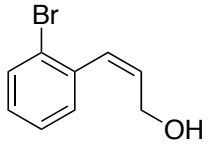
Naphthalene Precursor Synthesis

3-(2-Bromophenyl)prop-2-yn-1-ol (35)



Prepared according to a modified literature procedure.[168] To solution of 1,2-dibromobenzene (2.41 mL, 20.0 mmol) in *n*-$PrNH_2$ (60 mL, before Argon was passed through the solvent for 10 min) was added 2-propyn-1-ol (1.73 mL, 30.0 mmol) and $Pd(PPh_3)_4$ (693 mg, 600 µmol). The reaction mixture was refluxed (70 °C) for 28 h. 2-propyn-1-ol (1.15 mL, 20.0 mmol) was added again and the mixture was refluxed for 16 h. The solvent was removed *in vacuo* and the residue was purified by chromatography (pentane:Et_2O 7:3 to 3:7) to give a yellow liquid (2.42 g, 57%): R_f 0.20 (pentane:Et_2O 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (1H, dd, ^{3}J 8.0, ^{4}J 1.2, C3'*H*), 7.47 (1H, dd, ^{3}J 7.7, ^{4}J 1.7, C6'*H*), 7.26 (1H, ddd, ^{3}J 7.6, 7.6, ^{4}J 1.2, C5'*H*), 7.17 (1H, ddd, ^{3}J 7.7, 7.7, ^{4}J 1.7, C4'*H*), 4.55 (2H, d, ^{3}J 5.0, C*H*2), 1.82 (1H, t, ^{3}J 5.5, O*H*).
In agreement with literature data.[169]

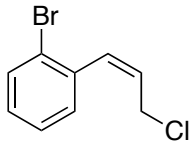
(*Z*)-3-(2-Bromophenyl)prop-2-en-1-ol (36)[170]



To a solution of $Ni(OAc)_2 \cdot 4\ H2O$ (2.86 g, 11.5 mmol) in EtOH (70 mL) at RT was added dropwise a solution of $NaBH_4$ (435 mg, 11.5 mmol) in EtOH (40 mL) and stirred for 1 h under a H_2-atmosphere. A solution of 3-(2-bromophenyl)prop-2-yn-1-ol (**35**, 2.30 g, 10.9 mmol) and ethylene-diamine (2.18 mL, 32.7 mmol) was added dropwise and the mixture was

stirred at RT for 4.5 h under a H_2-atmosphere. The solvent was removed *in vacuo*, the residue suspended in EtOAc and filtered through a plug of silica gel. The EtOAc was removed *in vacuo* and the residue was purified by chromatography (pentane:Et_2O 6:4) to give a yellow liquid 1.86 g, 80%): R_f 0.21 (pentane:Et_2O 6:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (1H, dd, ^3J 8.0 ^4J 1.2, C3'*H*), 7.29 (1H, ddd, ^3J 7.7, 7.5, ^4J 1.1, C5'*H*), 7.20 (1H, dd, ^3J 7.6, ^4J 1.8, C6'*H*), 7.14 (1H, ddd, ^3J 7.4, 7.4, ^4J 1.8, C4'*H*), 6.65 (1H, d, ^3J 11, C3*H*), 5.98 (1H, dt, ^3J 12, ^4J 6.7, C2*H*), 4.26–4.31 (2H, m, CH_2), 1.47 (1H, t, ^3J 5.7, O*H*). Minor impurity of (*E*)-isomer (approx. 5%).
In agreement with literature data.[171]

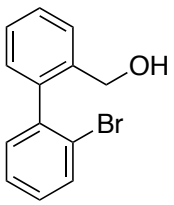
(*Z*)-1-Bromo-2-(3-chloroprop-1-en-1-yl)benzene (37)[172]



To a solution of LiCl (143 mg, 3.38 mmol) in DMF at 0 °C was added (*Z*)-3-(2-bromophenyl)prop-2-en-1-ol (**36**, 600 mg, 2.82 mmol), 2,6-lutidine (392 µL, 3.38 mmol) and slowly mesyl chloride (262 µL, 3.38 mmol). The reaction mixture was stirred at 0 °C for 3.5 h. Et_2O (20 mL) and H_2O (15 mL) were added. The phases were separated and the aq phase was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by chromatography (pentane:CH_2Cl_2 95:5 to 90:10) to give a colorless liquid (519 mg, 80%): R_f 0.42 (pentane), (*E*-isomer R_f 0.35). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (1H, dd, ^3J 8.0, ^4J 1.1, C6*H*), 7.30–7.40 (2H, m, C3*H*, C4*H*), 7.14–7.21 (1H, m, C5*H*), 6.69 (1H, d, ^3J 11, C1'*H*), 5.99 (1H, dt, ^3J 11, ^4J 8.1, C2'*H*), 4.13 (2H, d, ^3J 8.1, ^4J 1.0, CH_2).

Phenanthrene Precursor Synthesis

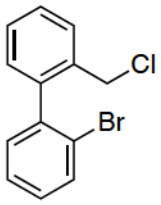
(2'-Bromo-[1,1'-biphenyl]-2-yl)methanol (39)



To a solution of 2,2'-dibromo-1,1'-biphenyl (prepared by R. Witzig, 1.00 g, 3.21 mmol) in THF (4.0 mL) at RT was added a solution of *i*-PrMgCl•LiCl (4.15 mL, 0.85 molL^{-1}, 3.53 mmol) and the reaction mixture was stirred at 50 °C for 5 h. A suspension of paraformaldehyde (116 mg, 3.85 mmol) in THF (4 mL) was added at RT and the reaction mixture was stirred at 50 °C for 12 h. Et_2O (20 mL), H_2O (20 mL) and an aq sat. solution of NH_4Cl (5.0 mL) were added. The phases were separated

and the aq phase was extracted with Et_2O (3 x 10 mL). The combined organic phases were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* (>50 mbar) and the residue was purified by chromatography (CH_2Cl_2) to give a colorless liquid, which crystallized over night to a white solid (518 mg, 61%): R_f 0.31 (CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (1H, d, ^3J 8.0), 7.58 (1H, d, ^3J 7.6), 7.44 (1H, ddd, ^3J 7.5, 7.5, ^4J 1.4), 7.36 (1H, dd, ^3J 7.5, 7.5, ^4J 1.2), 7.23–7.28 (2H, m), 7.15 (1H, dd, ^3J 7.5, ^4J 1.3), 4.50 (1H, dd, ^2J 12.9, ^3J 5.3, HC*H*), 4.41 (1H, dd, ^2J 12.9, ^3J 6.5, HC*H*), 1.59 (1H, t, ^3J 6.1, O*H*).
In agreement with literature data.[173]

2-Bromo-2'-(chloromethyl)-1,1'-biphenyl (40)[174]



To a solution of (2'-Bromo-[1,1'-biphenyl]-2-yl)methanol (**39**, 488 mg, 1.85 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added $SOCl_2$ (256 µL, 3.52 mmol) over 5 min. The reaction mixture was allowed to warm to RT and stirred for 2.5 h. H_2O (10 mL) and an aq sat. solution of $NaHCO_3$ (10 mL) were added. The phases were separated and the aq phase was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed *in vacuo* (>60 mbar) and the residue was purified by chromatography (pentane) to give a colorless liquid (384 mg, 74%): R_f 0.29 (pentane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (1H, dd, ^3J 8.0, ^4J 1.0), 7.56 (1H, dd, ^3J 7.5, ^4J 1.5), 7.32–7.46 (4H, m), 7.24–7.29 (1H, m), 7.18 (1H, dd, ^3J 7.4, ^2J 1.5), 4.48 (1H, d, ^2J 11.6, HC*H*), 4.30 (1H, d, ^2J 11.6, HC*H*).

Synthesis of Disubstituted Anthracenes and Anthrone

1,5-Bifunctional organomagnesium alkoxide reagent 46

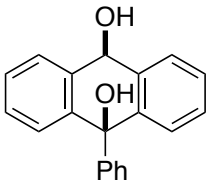
To a suspension of freshly cut magnesium turnings (48.1 mg, 1.98 mmol) in THF (1.5 mL) at RT. was added isopropylmagnesium chloride in THF (450 µL, 2 molL^{-1}, 900 µmol) and stirred for 5 min. A solution of bis(2-bromophenyl)methanol (**12**) (308 mg, 900 µmol) in THF (3.0 mL) was added and the reaction mixture was repeatedly heated to reflux until a change in color was observed. The mixture was stirred at 60 °C for 1 h and the reagent was directly used in the subsequent step.

Dialkoxide 50

A solution of methyl benzoate (81.7 mg, 600 µmol) in THF (3.0 mL) was directly added to a solution of **46** (prepared as described from 900 µmol of **12**) at 60 °C and stirred for 1 h at this temperature.

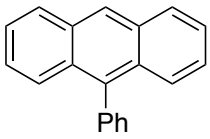
See specific compounds for the work-up procedures. Compounds **51** and **52** were prepared with 200 µmol methyl benzoate and the starting materials and solvent for the preparation of organomagnesium reagent **46** were adjusted to the corresponding reaction scale.

9-Phenyl-9,10-dihydroanthracene-9,10-diol (49)



A solution of dialkoxide **50** (prepared as described from 600 µmol methyl benzoate) at 0 °C was cannulated (and by this separated from residual Mg) into aq HCl (1.00 mL, 1.00 molL^{-1}). The mixture was vigorously stirred at 0 °C for 5 min. H_2O (5.0 mL) and Et_2O (15 mL) were added. The phases were separated and the aq phase was extracted with Et_2O (2 x 15 mL). The combined organic phases were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude was purified by chromatography (pentane:Et_2O 8:2 to 1:1) to give a white crystalline solid (172 mg, 99%, 140.8–145.2 °C): R_f 0.46 (pentane:Et_2O 1:1). ν_{max} (neat): 3519w, 3338m, 3063w, 3033w, 2361w, 2340w, 1599w, 1454m, 1373m, 1287w, 1246w, 1184m, 1129s, 1023s, 923m, 828w, 747s, 691s, 647s. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72–7.77 (2H, m, C1*H*, C8*H*), 7.64–7.70 (2H, m, C4*H*, C5*H*), 7.34–7.39 (4H, m, C2*H*, C3*H*, C6*H*, C7*H*), 7.16–7.21 (3H, m, C3'*H*, C4'*H*, C5'*H*), 7.08–7.12 (2H, m, C2'*H*, C6'*H*), 5.24 (1H, d, ^3J 9.4, C*H*OH), 2.94 (1H, s, C9O*H*), 2.47 (1H, d, ^3J 9.4, CHO*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.2 (*C1'*), 141.2 (*C8a, C9a*), 138.3 (*C4a, C10a*), 128.2 (*C3', C5'*), 127.8 (*C2, C7*), 127.7 (*C3, C6*), 127.5 (*C4'*), 126.8 (*C2', C6'*), 125.4 (*C1, C8*), 124.5 (*C4, C5*), 75.6 (*C9*), 68.1 (*C10*). HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{16}O_2Na$ 311.10425; found: 311.10408.

9-Phenylanthracene (51)



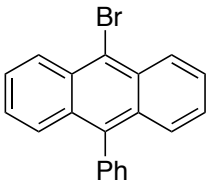
To the reaction solution of dialkoxide **50** (prepared as described from 200 µmol methyl benzoate) at RT was added aq HI (57%, 1.00 mL) and the mixture was vigorously stirred at RT for 13 h. Aq sat. $NaHCO_3$-solution (10 mL) and Et_2O (10 mL) were added. The phases were separated and the aq phase was extracted with Et_2O (2 x 10 mL). The combined organic phases were washed with aq sat. Na_2SO_3 (10 mL),

washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude was purified by chromatography (pentane) to give a beige solid (33.9 mg, 67%, 152.8–155.0 °C): R_f 0.22 (pentane).

ν_{max} (neat): 3051m, 3028w, 1809w, 1623w, 1596w, 1478w, 1442m, 1356m, 1260w, 1164m, 1072w, 1015m, 955w, 932m, 877m, 843m, 788m, 752m, 734s, 699s, 636m, 609s. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.49 (1H, s, C10*H*), 8.04 (2H, d, ^3J 8.5, C1*H*, C8*H*), 7.66 (2H, dd, ^3J 8.8, ^4J 0.9, C4*H*, C5*H*), 7.55–7.60 (2H, m, C3'*H*, C5'*H*), 7.50–7.54 (1H, m, C4'*H*), 7.41–7.47 (4H, m, C2*H*, C7*H*, C2'*H*, C6'*H*), 7.34 (2H, ddd, ^3J 8.8, 6.5, ^4J 1.3, C3*H*, C6*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.8 (*C1'*), 137.0 (*C9*), 131.4 (*C8a, C9a*), 131.2 (*C2'*), 130.2 (*C4a, C10a*), 128.4 (*C1, C8*), 128.3 (*C3'*), 127.4 (*C4'*), 126.8 (*C4, C5*), 126.5 (*C10*), 125.3 (*C3, C6*), 125.1 (*C2, C7*).

In agreement with literature data.[175]

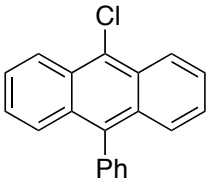
9-Bromo-10-phenylanthracene (52)



A solution of dialkoxide **50** (prepared as described from 200 µmol methyl benzoate) at 0 °C was cannulated (and by this separated from residual Mg) into a solution of BF_3 OEt_2 (103 µL, 400 µmol) in glacial AcOH (500 µL). The mixture was vigorously stirred at 60 °C for 1 h. H_2O (5.0 mL) and Et_2O (10 mL) were added. The phases were separated and the aq phase was extracted with Et_2O (2 x 10 mL). The combined organic phases were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude was purified by chromatography (pentane) to give a slightly yellow solid (43.6 mg, 65%, 147.9–151.2 °C): R_f 0.46 (pentane:CH_2Cl_2 9:1). ν_{max} (neat): 3073w, 3051w, 2326w, 1805w, 1620w, 1549w, 1438m, 1333m, 1258m, 1155w, 1087w, 1027m, 933s, 878m, 752s, 700s, 640s, 611s. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.61 (2H, ddd, ^3J 9.1, ^4J 1.1, ^5J 0.8, C1*H*, C8*H*), 7.64 (2H, ddd, ^3J 8.8, ^4J 1.1, ^5J 0.8, C4*H*, C5*H*), 7.54–7.61 (m, 5H), 7.35–7.42 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.4, 137.8, 131.1, 131.0, 130.2, 128.4, 127.8 (*C1, C8*), 127.7, 127.4 (*C4, C5*), 126.9, 125.5, 122.7.

In agreement with literature data.[176]

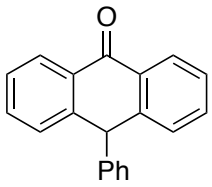
9-Chloro-10-phenylanthracene (53)



To a solution of 9-phenyl-9,10-dihydroanthracene-9,10-diol (**49**) (28.8 mg, 1.00 mmol) in toluene (1.0 mL) was added aq HCl (37%, 500 µL). The mixture was vigorously stirred at 100 °C for 13 h. H_2O (5.0 mL) and Et_2O (10 mL) were added. The phases were separated and the aq phase was extracted with Et_2O (2 x 10 mL). The combined organic phases were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude was purified by chromatography (pentane:CH_2Cl_2 9:1) to give a white solid (25.0 mg, 87%, 171.4–172.7 °C): R_f 0.51 (pentane:CH_2Cl_2 9:1). ν_{max} neat): 3073w (, 3053m, 2361w, 1923w, 1804w, 1620w, 1597w, 1551w, 1495w, 1438m, 1344s, 1282m, 1145w, 1069w, 1026m, 941s, 896m, 844w, 753s, 700s, 664m, 641s, 613s. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.58 (2H, d, ^3J 8.8, C1*H*, C8*H*), 7.65 (2H, d, ^3J 8.8, C4*H*, C5*H*), 7.53–7.60 (5H, m), 7.35–7.42 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.3, 136.8, 131.2, 130.7, 128.6, 128.5, 128.4, 127.7, 127.3 (*C4*, *C5*), 126.5, 125.5, 124.8 (*C1*, *C8*).

In agreement with literature data.[177]

10-Phenylanthracen-9(10H)-one (54)

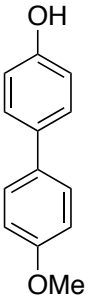


To a solution of 9-phenyl-9,10-dihydroanthracene-9,10-diol (**49**) (28.8 mg, 1.00 mmol) in THF (1.0 mL) was added aq $HClO_4$ (30%, 500 µL). The mixture was vigorously stirred at 60 °C for 1 h. H_2O (5.0 mL) and Et_2O (20 mL) were added. The phases were separated and the organic phase was washed with H_2O (2 x 5 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude was purified by chromatography (pentane:CH_2Cl_2 1:1) to give a beige solid (15.9 mg, 59%, decomp at 133.5 °C): R_f 0.36 (pentane:CH_2Cl_2 1:1). ν_{max} neat): 3026w, 3025w, 1972w, 1659s, 1600s, 1491w, 1453m, 1319s, 1173w, 1154w, 1092w, 966w, 930m, 813m, 750s, 703s, 679s, 616s. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.38 (2H, dd, ^3J 7.9, ^4J 1.4, C1*H*, C8*H*), 7.49 (2H, ddd, ^3J 7.5, 7.5, ^4J 1.5, C3*H*, C6*H*), 7.40–7.45 (2H, m, C2*H*, C7*H*), 7.23-7.30 (4H, m, C4*H*, C5*H*, C3'*H*, C5'*H*), 7.18–7.22 (1H, m, C4'*H*), 7.08–7.13 (2H, m, C2'*H*, C6'*H*), 5.42 (1H, s, C10*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 184.4 (*C9*), 144.4 (*C4a*, *C10a*), 144.1 (*C1'*), 133.2 (*C3*, *C6*), 131.1 (*C8a*, *C9a*), 129.7 (*C4*, *C5*), 129.0 (*C3'*, *C5'*), 128.9 (*C2'*, *C6'*), 127.3 (*C1*, *C8*), 127.2 (*C2*, *C7*), 126.9 (*C4'*), 48.4 (*C10*).

In agreement with literature data.[178]

The direct Ester to Phenol Transformation

4'-methoxy-[1,1'-biphenyl]-4-ol (Table 10, Entry 4)



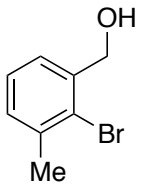
To a solution of (1*Z*,4*Z*)-1,5-diiodopenta-1,4-dien-3-ol (**57**) (101 mg, 300 µmol) in THF (1.0 mL) at –20 °C was added a solution of *n*-Bu_2Mg in *n*-heptane (366 µL, 0.41 $molL^{-1}$, 150 µmol) and the mixture was stirred for 10 min. The reaction mixture was cooled to –78 °C. A solution of *n*-BuLi in *n*-hexane (444 µL, 1.35 $molL^{-1}$, 600 µmol) was slowly added and the mixture was stirred for 15 min at –78 °C. A solution of methyl anisate (24.9 mg, 150 µmol) in THF (1.0 mL) was slowly added and the reaction mixture was stirred while slowly warming up to 0 °C over 4 h. Aqueous HCl (2.0 mL, 1.00 $molL^{-1}$) was added and the mixture was extracted with Et_2O (2 x 5.0 mL). The organic layers were washed with brine (3.0 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and was purified by chromatography (Et_2O:pentane 20:80 to 30:70) to give the desired product as a white solid (3.50 mg, 12%): R_f 0.39 (Et_2O:pentane 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.49 (4H, m, C2*H*, C6*H*, C2'*H*, C6'*H*), 6.93–6.98 (2H, m, C3'*H*, C5'*H*), 6.83–6.91 (2H, m, C3*H*, C5*H*), 4.85 (1H, s, O*H*), 3.84 (3H, s, CH_3).

In agreement with literature data.[179]

Studies on the Stereoselective Transformation of Esters into Substituted Chiral Anthracenes

Precursor Synthesis

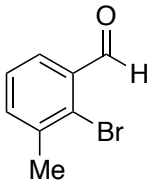
(2-Bromo-3-methylphenyl)methanol (71)



To a solution of 2-bromo-3-methylbenzoic acid (5.00 g, 23.3 mmol) in anh. THF (50 mL) at 0 °C was added BH_3 SMe_2 (14.0 mL, 2.00 $molL^{-1}$, 28.0 mmol) over 5 min (Caution Gas evolution!). The reaction mixture was refluxed for 1 h. The reaction mixture was cooled to 0 °C and H_2O (50 mL) was slowly added (Caution Gas evolution!). The mixture was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo* to give a white solid (4.65 g, 99%, m.p. 75.1–77.4 °C): R_f 0.15 (pentane:Et_2O 8:2); ν_{max} (neat): 3314s, 2974w, 2919m, 2858w,

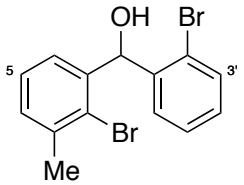
1927w, 1856w, 1785w, 1664w, 1578w, 1452s, 1408s, 1373s, 1350m, 1241s, 1169m, 1058s, 1025s, 997s, 901m, 768s, 644s, 622s; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16–7.31 (3H, m, C4*H*, C5*H*, C6*H*), 4.75 (2H, s, CH_2), 2.42 (3H, s, CH_3), 2.13 (1H, br, O*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.1 (*C1*), 138.5 (*C3*), 130.0 (*C4*), 127.2 (*C5*), 126.3 (*C6*), 125.2 (*C2*), 65.7 (*C*HOH), 23.2 (*C*H_3); ESI-MS: m/z calcd. for $C_8H_9BrNaO^+$ 222.9729 found 222.9729 [M+Na^+].

2-Bromo-3-methylbenzaldehyde (72)



Prepared according to a modified literature procedure.[180] A suspension of (2-Bromo-3-methylphenyl)methanol (6.02 g, 29.9 mmol) and MnO_2 (13.0 g, 150 mmol) in CH_2Cl_2 (200 mL) was sonificated at RT for 10 min and stirred for 84 h at RT. The suspension was filtered over a plug of celite and the solvent was removed *in vacuo* to give yellow crystals (5.71 g, 96%, m.p. 49.6–54.5 °C): R_f 0.31 (pentane:Et_2O 9:1); ν_{max} (neat): 3340w, 2982m, 2867m, 2360w, 1952w, 1890w, 1826w, 1674s, 1572s, 1450s, 1373s, 1237s, 1168m, 1105m, 1031s, 1007m, 911s, 779s, 690s; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.45 (1H, d, ^{4}J 0.8, C*H*O), 7.74 (1H, ddd, ^{3}J 7.7, ^{4}J 1.8, 0.6, C6*H*), 7.48 (1H, ddd, ^{3}J 7.4, ^{4}J 1.8, 0.7, C4*H*), 7.32 (1H, dd, ^{3}J 7.6, 7.6, C5*H*), 2.48 (3H, s, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.7 (*C*HO), 139.6 (*C3*), 136.3 (*C4*), 134.0 (*C1*), 129.6 (*C2*), 127.4 (*C6*), 127.3 (*C5*), 22.9 (*C*H_3).

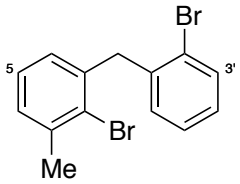
(2-Bromo-3-methylphenyl)(2-bromophenyl)methanol (73):[109]



To a solution of 1,2-dibromobenzene (4.08 mL, 33.8 mmol) in anhydrous THF (30 mL) at –15 °C was added isopropylmagnesium chloride lithium chloride complex in THF (26.0 mL, 1.30 $molL^{-1}$, 33.8 mmol) over 20 min and the reaction mixture was stirred for 2 h at the same temperature. A solution of 2-bromo-3-methylbenzaldehyde (5.61 g, 28.2 mmol) in anhydrous THF (30 mL) was added at –15 °C over 30 min and the reaction mixture was stirred for 1 h at the same temperature. An aqueous saturated solution of NH_4Cl (60 mL) and H_2O (40 mL) was added and the reaction mixture was allowed to warm to RT. The mixture was extracted with Et_2O (3 x 50 mL), the combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo*

to give a yellow solid. The solid was resuspended in pentane (20 mL), followed by removal of the supernatant (2 times) to give a beige solid (9.43 g, 94%, m.p. 91.7–97.0 °C): R_f 0.29 (pentane:Et_2O 8:2); ν_{max} (neat): 3542m, 3459m, 3066w, 2956w, 2925w, 2361w, 1571w, 1462m, 1436s, 1379w, 1273w, 1196m, 1108w, 1017s, 918w, 780s, 756s, 683m, 615s; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.59 (1H, m, C3'*H*), 7.26–7.33 (2H, m, C5'*H*, C6'*H*), 7.19–7.21 (2H, m, C4*H*, C5*H*), 7.13–7.19 (2H, m, C6*H*, C4'*H*), 6.45 (1H, d, ^3J 4.1, C*H*OH), 2.60 (1H, d, ^3J 4.2, O*H*), 2.43 (3H, s, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.3 (*C1*), 141.2 (*C1'*), 138.8 (*C3*), 132.9 (*C3'*), 130.4 (*C4*), 129.3 (*C4'*), 128.7 (*C6'*), 127.6 (*C5'*), 127.1 (*C5*), 126.3 (*C2*), 126.0 (*C6*), 124.0 (*C2'*), 74.7 (*C*HOH), 23.7 (*C*H_3); ESI-MS: m/z calcd. for $C_{14}H_{12}Br_2NaO^+$ 376.9147 found 376.9140 [M+Na^+].

2-Bromo-1-(2-bromobenzyl)-3-methylbenzene (74):[110]



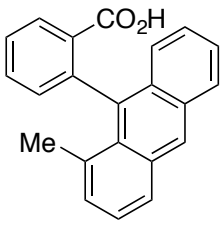
To a suspension of (2-bromo-3-methylphenyl)(2-bromophenyl)-methanol (9.12 g, 25.6 mmol) and anhydrous sodium iodide (7.67 g, 51.2 mmol) in MeCN (40 mL) at RT was added TMSCl (6.18 mL, 51.2 mmol) over 10 min. The mixture was stirred for 71 h** at RT. An aqueous saturated solution of Na_2SO_3 (50 mL) and H_2O (50 mL) was added and the mixture was extracted with pentane (3 x 50 mL), the combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo* to give a purple oil. Purification by chromatography (pentane) gave a white solid (5.94 g, 68%, m.p. 32.4–35.1 °C): R_f 0.38 (pentane); ν_{max} (neat): 3051w, 2985w, 2945w, 2921w, 2902w, 2361w, 2340w, 1933w, 1789w, 1587w, 1563w, 1462s, 1436s, 1323w, 1270w, 1246w, 1159m, 1108w, 1020s, 953m, 912m, 810m, 787s, 762s, 739s, 665m, 636m; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (1H, dd, ^3J 7.9, ^4J 1.3, C3'*H*), 7.20 (1H, ddd, ^3J 7.5, 7.5, ^4J 1.3, C5'*H*), 7.07–7.15 (3H, m, C4*H*, C5*H*, C4'*H*), 6.96 (1H, dd, ^3J 7.6, ^4J 1.6, C6'*H*), 6.78–6.82 (1H, m, C6*H*), 4.22 (2H, s, CH_2), 2.45 (3H, s, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.2 (*C1'*), 139.1 (*C1*), 138.8 (*C3*), 132.8 (*C3'*), 130.6 (*C6'*), 129.0 (*C4*), 128.1 (*C6*), 128.0 (*C4'*), 127.7 (*C2*), 127.5 (*C5'*), 126.9 (*C5*), 125.1 (*C2'*), 42.9 (*C*H_2), 24.0 (*C*H_3).

1,5-Bifunctional Diarylmagnesium Reagent 19 (Me-substituted Anthracenes):

Representative Scale:

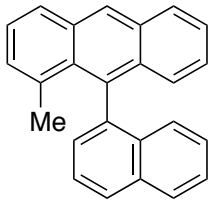
To a suspension of magnesium turnings (23.3 mg, 960 µmol) in anhydrous THF (0.4 mL) at RT was added a solution of 2-bromo-1-(2-bromobenzyl)-3-methylbenzene (**74**, 136 mg, 400 µmol) in anhydrous THF (1.0 mL). The mixture was repeatedly heated to mild reflux until a change in color was observed. The mixture was stirred at RT for 2 h. Analysis of an aliquot with GC-MS confirmed full exchange. The reagent was used directly without titration in the next step.

2-(1-Methylanthracen-9-yl)benzoic acid



A solution of dimethyl phthalate (100 µmol) in anhydrous THF (1.00 mL) at RT was treated with reagent **19** in THF (approx. 400 µmol) and stirred at RT for 3 h. Aqueous HCl (2.50 mL, 1.00 molL^{-1}) was added and the mixture was extracted with Et_2O (6 x 1.0 mL). The organic layers were washed with brine (1.0 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was triturated with n-pentane (7 mL) to yield a white solid (23.3 mg, 75%): ^{1}H NMR (500 MHz, $CDCl_3$, low solubility): δ = 8.49 (1H, s, C10*H*), 8.16–8.21 (1H, m), 8.00 (1H, dd, ^3J 8.4, ^4J 1.0), 7.94 (1H, d, ^3J 7.9), 7.57–7.65 (2H, m), 7.38–7.43 (1H, m), 7.30–7.35 (2H, m), 7.22–7.26 (1H, m), 7.15–7.20 (2H, m), 1.98 (3H, s, C*H*$_3$), 0.80–2.13 (br, CO_2H).

1-Methyl-9-(naphthalen-1-yl)anthracene

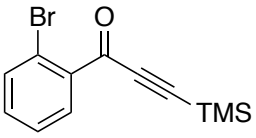


A solution of methyl 1-naphthoate (40 µmol) in anhydrous THF (1.00 mL) at RT was treated with reagent **19** in THF (approx. 50 µmol) and stirred at RT for 18 h. Aqueous HCl (2.50 mL, 1.00 molL^{-1}) was added and the mixture was extracted with Et_2O (6 x 1.0 mL). The organic layers were washed with brine (1.0 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and was purified by chromatography (pentane) to give a beige solid (6.82 mg, 54%): R_f 0.13 (pentane); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (1H, s, C10*H*), 7.95–8.06 (4H, m), 7.60 (1H, dd, ^3J 8.2, 7.1), 7.38–7.48 (3H, m), 7.33 (1H, dd, ^3J 8.4, 6.8), 7.10–7.24 (5H, m), 1.72 (3H, s, C*H*$_3$).

The Direct Transformation of Esters in Axially Chiral TMS-Naphthalenes

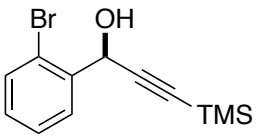
A. Synthesis of Reagent Precursors

1-(2-Bromophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (102)



To a solution of trimethylsilylacetylene (74.0 mL, 520 mmol) in THF (240 mL) at 0 °C was added a solution of isopropylmagnesium chloride in THF (255 mL, 2.00 molL^{-1}, 510 mmol) over 40 min and the mixture was stirred for 15 min at this temperature. 2-bromobenzaldehyde (59.7 mL, 500 mmol) was added over 15 min and the mixture was stirred for 15 min at 0 °C. An aqueous saturated solution of NH_4Cl (300 mL) and H_2O (400 mL) was added. The mixture was extracted with Et_2O (4 x 300 mL), the combined organic phases were washed with brine (200 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue (142 g) was dissolved in EtOAc (500 mL), MnO_2 (98.8 g, 88%, 1.00 mol) was added and the mixture was stirred at 75 °C for 2.5 h. MnO_2 (49.4 g, 500 mmol) was added and the mixture was stirred at 75 °C. After 2.5 h MnO_2 (49.4 g, 500 mmol) was added again and the reaction was stirred at the same temperature for 2.5 h. The suspension was filtered over a plug of celite, the plug was purged with EtOAc (1 L) and the solvent was removed in vacuo to give 1-(2-bromophenyl)-3-(trimethylsilyl)prop-2-yn-1-one as a yellow liquid (140 g, 99% over 2 steps):): R_f 0.57 (*n*-pentane:Et_2O 95:5); ν_{max} (neat): 3067w, 2962m, 2901w, 2153m, 1654s, 1586m, 1463w, 1432m, 1274m, 1231s, 1165w, 1130w, 1066m, 1008s, 841s, 761m, 737s, 705w, 679m, 625m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.04 (1H, dd, ^3J 7.7, ^4J 1.8, C6'*H*), 7.68 (1H, dd, ^3J 7.9, ^4J 1.2, C3'*H*), 7.43 (1H, ddd, ^3J 7.6, 7.6, ^4J 1.3, C5'*H*), 7.37 (1H, ddd, ^3J 7.9, 7.9, ^4J 1.8, C4'*H*), 0.29 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 177.0 (*C1*), 136.8 (*C1'*), 135.0 (*C3'*), 133.4 (*C4'*), 133.2 (*C6'*), 127.3 (*C5'*), 121.3 (*C2'*), 101.7 (*C3*), 101.5 (*C2*), –0.81 (Si(*C*H3)3); ESI-MS: m/z calcd. for $C_{12}H_{13}BrSiOH^{\cdot+}$ 280.9992 found 280.9989 [$MH^{\cdot+}$].

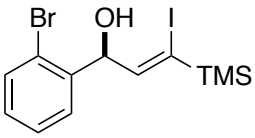
(*S*)-1-(2-Bromophenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (98)



The solvent from a commercial available (Sigma-Aldrich 232734) *R*-Alpine-Borane®-solution in THF (140 mL, 0.500 molL^{-1}, 70.0 mmol) was removed *in vacuo* (<10 mbar, 30 °C) for 15 min. To the residue under Argon at RT (cool reaction with water bath) was added 1-(2-

bromophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (14.1 g, 50.0 mmol) over 10 min and the mixture was stirred at RT for 24 h. Propionaldehyde (1.79 mL, 25.0 mmol) was added at 0 °C and the mixture was stirred for 5 min. The volatiles were removed *in vacuo*. The residue was dissolved in anhydrous Et_2O (60 mL), ethanolamine (9.06 mL, 150 mmol) was added at 0 °C and the mixture was stirred for 15 min at this temperature. The suspension was filtered over a plug of celite, the plug was purged with cold Et_2O (2 x 15 mL). To the filtrate was added Et_2O (100 mL) and the organic solution was washed with brine (3 x 20 mL), dried over Na_2SO_4 and the solvent was removed *in vacuo*. Purification by chromatography (*n*-pentane:Et_2O 95:5 to 80:20) gave a clear liquid (12.9 g, 91%, e.r. 98:2 by HPLC): R_f 0.18 (*n*-pentane:Et_2O 95:5); $[\alpha]_D$ –24.1 (c 1.00, $CHCl_3$); ν_{max} (neat): 3372m, 3067w, 2960m, 2899w, 2174m, 1698w, 1571w, 1469m, 1440m, 1411w, 1298w, 1249s, 1191w, 1122w, 1026s, 983s, 838s, 753s, 698m, 661m, 629m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (1H, dd, ^3J 7.7, ^4J 1.7, C6'*H*), 7.56 (1H, dd, ^3J 8.0, ^4J 1.2, C3'*H*), 7.37 (1H, ddd, ^3J 7.6, 7.6, ^4J 1.2, C5'*H*), 7.20 (1H, ddd, ^3J 7.9, 7.9, ^4J 1.7, C4'*H*), 5.78 (1H, d, ^3J 3.7, C1*H*), 2.45 (1H, d, ^3J 4.7, C1O*H*), 0.20 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.2 (*C1'*), 133.0 (*C3'*), 130.0 (*C4'*), 128.7 (*C6'*), 127.9 (*C5'*), 123.0 (*C2'*), 103.6 (*C2*), 92.1 (*C3*), 64.6 (*C1*), –0.22 (Si(*C*H_3)$_3$); ESI-MS: m/z calcd. for $C_{12}H_{14}BrSiOHNa$ 304.9968 found 304.9965 [$MNa^{\cdot+}$]. The e.r. was determined by HPLC using a Chiralcel OJ-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 10:90): (+)-(*R*)-**98** t_R = 5.08 min and (–)-(*S*)-**98** t_R = 5.70 min.

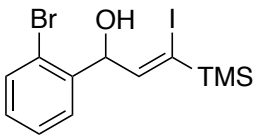
(*S*,*Z*)-1-(2-Bromophenyl)-3-iodo-3-(trimethylsilyl)prop-2-en-1-ol (99)



To a solution of (*S*)-1-(2-bromophenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (12.7 g, 45.0 mmol) in THF (180 mL) at 0 °C was added a solution of isopropyl-magnesium chloride in THF (23.6 mL, 2.00 molL^{-1}, 47.3 mmol) over 10 min. Red-Al® in toluene (16.7 mL, 3.50 molL^{-1}, 58.5 mmol) was added at 0 °C over 30 min and the mixture was stirred for 2 h at this temperature. The reaction mixture was cooled to –35 °C, EtOAc (22.0 mL, 225 mmol) was added over 20 min and the mixture was stirred for 1 h at this temperature. A solution of iodine (28.6 g, 112 mmol) in THF (120 mL) was added at –35 °C over 30 min, the mixture was stirred for 10 min at this temperature. The reaction mixture was warmed to 0 °C with an ice-water-bath and allowed to warm to RT over 13 h. An aqueous saturated solution

of Rochelle-salt (150 mL) and H_2O (150 mL) was added and the mixture vigorously stirred for 30 min. An aqueous saturated solution of Na_2SO_3 (30 mL) was added and the mixture was extracted with Et_2O (3 x 150 mL). The combined organics were washed with brine (50 mL), dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. Purification by chromatography (*n*-pentane:Et_2O 95:5 to 80:20) gave a liquid with side product and residual starting material inside. These were removed at 110 °C *in vacuo* (1.5 x 10^{-2} mbar) to give the pure desired compound as a clear yellow liquid (14.2 g, 77%, e.r. 98:2 by HPLC): R_f 0.15 (*n*-pentane:Et_2O 95:5); $[\alpha]_D$ +114.0 (c 1.00, $CHCl_3$); ν_{max} (neat): 3371m, 3065w, 2957m, 2897w, 2362w, 2334w, 1590w, 1569w, 1469m, 1437m, 1407w, 1293w, 1247s, 1191m, 1121w, 1007s, 945w, 890s, 836s, 750s, 677m, 626m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.59 (2H, m, C3'*H*, C6'*H*), 7.35 (1H, ddd, ^{3}J 7.6, 7.6, ^{4}J 1.2, C5'*H*), 7.18 (1H, ddd, ^{3}J 7.7, 7.7, ^{4}J 1.7, C4'*H*), 6.50 (1H, d, ^{3}J 6.9, C2*H*), 5.71 (1H, dd, ^{3}J 6.9, 3.8, C1*H*), 2.45 (1H, d, ^{3}J 3.8, C1O*H*), 0.20 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 146.7 (*C2*), 140.7 (*C1'*), 133.0 (*C3'*), 129.4 (*C5'*), 128.5 (*C6'*), 127.8 (*C4'*), 123.0 (*C2'*), 116.8 (*C3*), 78.6 (*C1*), –1.55 (Si(*C*H$_3$)$_3$); ESI-MS: m/z calcd. for $C_{12}H_{16}BrINaOSi$ 432.9091 found 432.9088 [$MNa^{\cdot+}$]; The e.r. was determined by HPLC using a Chiralcel OJ-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 2:98): (–)-(*R*)-**99** t_R = 8.98 min and (+)-(*S*)-**99** t_R = 9.72 min.

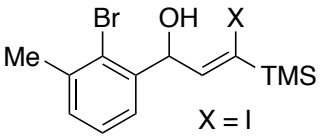
(*Z*)-1-(2-Bromophenyl)-3-iodo-3-(trimethylsilyl)prop-2-en-1-ol (94)



To a solution of trimethylsilylacetylene (14.8 mL, 104 mmol) in THF (100 mL) at 0 °C was added a solution of isopropylmagnesium chloride in THF (51 mL, 2.00 molL^{-1}, 102 mmol) over 10 min and the mixture was stirred for 15 min at this temperature. 2-bromobenzaldehyde (11.7 mL, 100 mmol) was added over 10 min and the mixture was stirred for 15 min at 0 °C. Red-Al® in toluene (37.1 mL, 3.50 molL^{-1}, 130 mmol) was added at 0 °C over 30 min and the mixture was stirred for 135 min at this temperature. The reaction mixture was cooled to –35 °C, EtOAc (48.8 mL, 500 mmol) was added over 50 min and the mixture was stirred for 1 h at this temperature. A solution of iodine (63.5 g, 250 mmol) in THF (160 mL) was added at –35 °C over 1 h, the mixture was stirred for 10 min at this temperature. The reaction mixture was warmed to 0 °C with an ice-water-bath and allowed to warm to RT over 13 h. An aqueous saturated solution of Rochelle-salt (150 mL) and H_2O (150 mL) was added and the mixture

vigorously stirred for 30 min. An aqueous saturated solution of Na_2SO_3 (100 mL) was added and the mixture was extracted with Et_2O (3 x 200 mL). The combined organics were washed with brine (50 mL), dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. Purification by recrystallization in *n*-heptane (30 mL) at −20 °C over night gave purple crystals (29.5 g, 72%, m.p. 38.0–39.5 °C). NMR same as above.

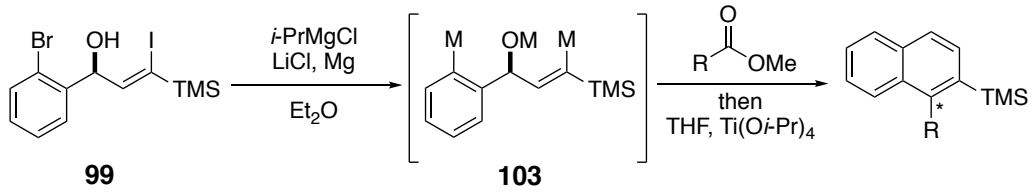
(*Z*)-1-(2-Bromo-3-methylphenyl)-3-iodo-3-(trimethylsilyl)prop-2-en-1-ol (105)



To a solution of trimethylsilylacetylene (1.57 mL, 11 mmol) in THF (10 mL) at 0 °C was added a solution of isopropylmagnesium chloride in THF (5.47 mL, 1.92 molL^{-1}, 10.5 mmol) over 5 min and the mixture was stirred for 15 min at this temperature. A solution of 2-bromo-3-methylbenzaldehyde (1.99 g, 10 mmol) in THF (20 mL) was added over 10 min and the mixture was stirred for 15 min at 0 °C. Red-Al® in toluene (3.71 mL, 3.50 molL^{-1}, 13.0 mmol) was added at 0 °C over 15 min and the mixture was stirred for 2 h at this temperature. The reaction mixture was cooled to −35 °C, EtOAc (4.88 mL, 50 mmol) was added over 20 min and the mixture was stirred for 1 h at this temperature. A solution of iodine (6.35 g, 25 mmol) in THF (25 mL) was added at −35 °C over 20 min, the mixture was stirred for 10 min at this temperature. The reaction mixture was warmed to 0 °C with an ice-water-bath and allowed to warm to RT over 16 h. An aqueous saturated solution of Rochelle-salt (50 mL) and H_2O (50 mL) was added and the mixture vigorously stirred for 10 min. An aqueous saturated solution of Na_2SO_3 (10 mL) was added and the mixture was extracted with Et_2O (2 x 50 mL). The combined organics were washed with brine (15 mL), dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. Purification by recrystallization in *n*-heptane (20 mL) at −20 °C over night gave purple crystals (2.12 g, 50%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39 (1H, dd, ^3J 7.5, ^4J 1.9), 7.19–7.26 (2H, m), 6.50 (1H, d, ^3J 6.8, C2*H*), 5.76 (1H, d, ^3J 6.8, C1*H*), 2.44 (3H, s, CH_3), 2.14–2.57 (1H, br. s, O*H*), 0.20 (9H, s, Si(CH_3)$_3$)

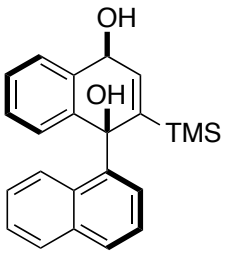
B. Stereoselective Direct Ester to Arene Transformation

General procedure D for the direct stereoselective transformation of Esters into axially chiral Biaryls:



A mixture of Mg-powder (72.9 mg, 3.00 mmol) and dry LiCl (27.1 mg, 0.639 mmol) was dry stirred under vacuum (1.3 x 10^{-1} mbar) and heated with the heatgun for 1 min. Under stirring, the mixture was allowed to cool to RT (5-10 min) under vacuum and the flask was flushed with argon. Et_2O (2 mL) and a solution of *i*-PrMgCl in Et_2O (125 µL, 2.00 molL^{-1}, 250 µmol) were added. To this mixture was added a solution of (*S*,*Z*)-1-(2-Bromophenyl)-3-iodo-3-(trimethylsilyl)prop-2-en-1-ol (**99**) (103 mg, 250 µmol) in Et_2O (2 mL) (**Caution gas evolution!**). The reaction mixture was warmed to 40 °C and after the solution turned yellow (indication of start of the metalation, usually about 5 min) the reaction mixture was stirred for 45 min at 40 °C. The mixture was cooled to RT, a solution of the specified ester (200 µmol) in Et_2O (2 mL) was added and the reaction was stirred for 1 h at RT. THF (4 mL) was added, the mixture stirred for 5 min and then Ti(*i*-OPr)$_4$ (180 µL, 600 µmol) was added. The reaction mixture was stirred for 3 h (or for 1 h, specified below) at RT. The mixture was cooled to 0 °C, an aqueous HCl-solution (1 molL^{-1}, 20 mL) and Et_2O (25 mL) was added. The phases were separated and the aqueous phase was extracted with Et_2O (25 mL). The combined organics were washed with aqueous saturated $NaHCO_3$-solution (5 mL), dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography as specified in the individual examples.

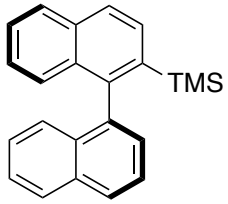
(1*S*,4*S*)-2-(Trimethylsilyl)-[1,1'-binaphthalene]-1,4(4*H*)-diol (Table 13, entry 3)



Prepared according to general procedure **D** using methyl 1-naphthoate (37.2 mg, 200 µmol), **in situ reduction in Et_2O (without THF addition).** Workup with aqueous HCl-solution (1 molL^{-1}) as described above. Trituration of crude residue with *n*-pentane (3 x 2 mL) to give a white solid (46.2 mg, 64%, e.r. 98:2 by HPLC) ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.33 (1H, dd, ^3J 7.3, ^4J 1.3, C2'*H*), 7.82 (1H, d, ^3J 8.2, C4'*H*), 7.77 (1H, dd, ^3J 8.4, ^4J 1.4, C5'*H*), 7.55–7.63 (2H, m, C6*H*, C3'*H*), 7.27–7.31 (2H, m, C6'*H*, C8'*H*), 7.23–7.27 (1H, m, C6*H*), 7.11 (1H, ddd, ^3J 8.6, 6.9, ^4J 1.5, C7'*H*), 7.03–7.08 (1H, m, C7*H*), 6.99 (1H, dd, ^3J 8.0, ^4J 1.3, C8*H*), 6.63 (1H, d, ^3J 6.6, C3*H*), 5.33 (1H, dd,

^{3}J 7.3, 3.5, C4*H*), 2.47 (1H, s, C1O*H*), 2.30 (1H, d, ^{3}J 8.0, C4O*H*), –0.38 (Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 147.7 (*C2*), 142.5 (*C8a*), 140.0 (*C1'*), 137.7 (*C3*), 134.4 (*C4a*), 134.3 (*C4'a*), 130.4 (*C8a'*), 128.8 (*C4'*), 128.7 (*C5'*), 128.6 (*C7*), 128.1 (*C5*), 127.8 (*C6*), 127.7 (*C8*), 125.2 (*C7'*), 125.1 (*C6'*), 124.9 (*C8'*), 124.8 (*C3'*), 124.5 (*C2'*), 73.7 (*C1*), 65.2 (*C4*), –0.47 (Si*C*H$_3$)$_3$); ESI-MS: m/z calcd. for $C_{23}H_{24}NaO_2Si$ 383.1443 found 383.1443 [$MNa^{\cdot+}$]; The e.r. was determined by HPLC using a Chiralcel OD-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 5:95): (*R*,*R*)-Diol t_R = 5.68 min and (*S*,*S*)-Diol t_R = 7.00 min.

(*R*$_a$)-[1,1'-Binaphthalen]-2-yltrimethylsilane (88a)

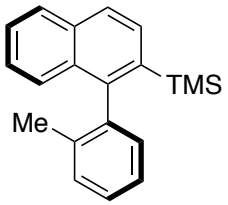


Prepared according to general procedure **D** using methyl 1-naphthoate (37.2 mg, 200 µmol), chromatography with *n*-pentane to give a white solid (53.2 mg, 82%, e.r. 98:2 by HPLC, m.p. 79.0–80.9 °C): R_f 0.40 (*n*-pentane); $[\alpha]_D$ + 81.0 (c 1.00, $CHCl_3$); ν_{max} (neat): 3048m, 2953m, 2895w, 1926w, 1590w, 1552w, 1502m, 1454w, 1405w. 1354m, 1315w, 1248s, 1165w, 1107m, 1024m, 947m, 876s, 831s, 780s, 756s, 687s, 640m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.01 (1H, ddd, ^{3}J 8.3, ^{4}J 1.1, 1.1, C4'*H*), 7.96–8.00 (2H, m, C4*H*), 7.94 (1H, ddd, ^{3}J 8.2, ^{4}J 1.1, 1.1, C5*H*), 7.85 (1H, d, ^{3}J 8.3, C3*H*), 7.63 (1H, dd, ^{3}J 8.3, 6.9, C3'*H*), 7.46–7.52 (3H, m, C2'*H*), 7.20–7.31 (4H, m), –0.15 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.9 (*C1*), 139.2 (*C1'*), 137.5 (*C2*), 134.1 (*C8a'*), 133.6 (*C4a*), 133.4 (*C4a'*), 133.2 (*C8a*), 130.8 (*C3*), 128.7 (*C2'*), 128.13 (*C4*), 128.10 (*C4'*), 127.8 (*C5*), 127.1, 127.0, 126.8, 126.2, 126.03, 125.99, 125.91, 125.2 (*C3'*), 0.21 (Si(*C*H$_3$)$_3$); The e.r. was determined by HPLC using a Chiralcel OD-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (+)-(*R*)-**88a** t_R = 5.90 min and (–)-(*S*)-**88a** t_R = 7.47 min.

2.00 mmol scale

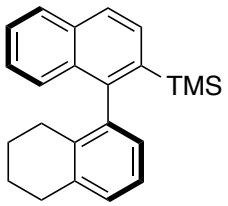
Prepared according to general procedure **D** using methyl 1-naphthoate (372 mg, 2.00 mmol), chromatography with *n*-pentane:Et_2O (100:0 to 95:5) to give a white solid (500 mg, 77%, e.r. 98:2 by HPLC)

(*R*$_a$)- (1-(*o*-Tolyl)naphthalen-2-yl)trimethylsilane (88b)



Prepared according to general procedure **D** using methyl 2-methylbenzoate (30.0 mg, 200 µmol), chromatography with *n*-pentane to give a colorless solid (46.3 mg, 80%, e.r. 98:2 by HPLC, m.p. 51.5–53.4 °C): R_f 0.56 (*n*-pentane); $[\alpha]_D$ + 52.8 (c 0.50, $CHCl_3$); ν_{max} (neat): 3058w, 2953m, 2896w, 1550w, 1486w, 1453w, 1360w, 1313w, 1247m, 1163w, 1113w, 1095w, 1025w, 968w, 875m, 823s, 757s, 734s, 687m, 646m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.81–7.86 (2H, m, C4*H*, C5*H*), 7.71 (1H, d, ^3J 8.3, C3H), 7.44 (1H, ddd, ^3J 8.1, 6.7, ^4J 1.4, C6*H*), 7.35 (1H, ddd, ^3J 7.5, 7.5, ^4J 1.5, C4'*H*), 7.24–7.33 (4H, m, C7*H*, C8*H*, C3'*H*, C5'*H*), 7.17 (1H, dd, ^3J 7.4, ^4J 1.6, C6'*H*), 1.90 (3H, s, CH_3), –0.01 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 146.2 (*C1*), 140.8 (*C1'*), 137.6 (*C2'*), 135.7 (*C2*), 133.5 (*C4a*), 132.0 (*C8a*), 131.0 (*C6'*), 130.7 (*C3*), 129.6 (*C3'*), 127.81 (*C4*), 127.77 (*C4'*), 126.3 (*C5*), 126.2 (*C7*), 126.1 (*C6*), 125.9 (*C8*), 125.3 (*C5'*), 20.0 (*C*H$_3$), 0.03 (Si(*C*H$_3$)$_3$); The e.r. was determined by HPLC using a Chiralpak AD-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (+)-(*R*)- **88b** t_R = 3.72 min and (–)-(*S*)- **88b** t_R = 3.95 min.

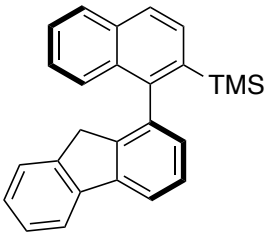
(*R*$_a$)- (5',6',7',8'-Tetrahydro-[1,1'-binaphthalen]-2-yl)trimethylsilane (88c)



Prepared according to general procedure **D** using methyl 5,6,7,8-tetrahydronaphthalene-1-carboxylate (38.0 mg, 200 µmol), chromatography with *n*-pentane to give a colorless gel (44.9 mg, 68%, e.r. 98:2 by HPLC): R_f 0.54 (*n*-pentane); $[\alpha]_D$ + 58.6 (c 0.50, $CHCl_3$); ν_{max} (neat): 3052w, 2948m, 2927m, 2859m, 1940w, 1585w, 1551w, 1499w, 1451m, 1378w, 1330w, 1246m, 1169w, 1104w, 1023w, 972w, 945w, 871s, 834s, 820s, 780m, 756s, 680w, 663m, 641w; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.79–7.84 (2H, m, C4*H*, C5*H*), 7.70 (1H, d, ^3J 8.4, C3*H*), 7.40–7.46 (1H, m, C6*H*), 7.28–7.32 (2H, m, C7*H*, C8*H*), 7.13–7.20 (2H, m, C3'*H*, C4'*H*), 6.98 (1H, dd, ^3J 6.7, ^4J 2.1, C2'*H*), 2.81–2.93 (2H, m, C5'H_2), 2.06–2.26 (2H, m, C8'H_2), 1.67–1.80 (2H, m, C6'H_2), 1.52–1.65 (2H, m, C7'H_2), –0.01 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 146.5 (*C1*), 140.6 (*C1'*), 137.0 (*C4a'*), 136.5 (*C8a'*), 135.4 (*C2*), 133.5 (*C4a*), 132.0 (*C8a*), 130.8 (*C3*), 128.7 (*C4'*), 128.3 (*C2'*), 127.8 (*C4*), 126.2 (*C5*), 126.1 (*C8*), 126.0 (*C7*), 125.9 (*C6*), 124.8 (*C3'*), 30.0 (*C5'*), 27.3 (*C8'*), 23.1 (*C6'*), 23.0 (*C7'*), 0.05 (Si(*C*H$_3$)$_3$); The e.r. was determined by HPLC using a Chiralcel OD-H column (1.00 mLmin^{-1}, *i*-

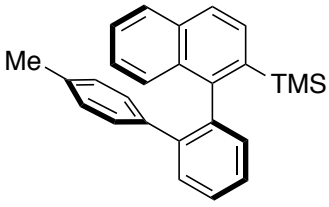
PrOH:*n*-heptane 0.2:99.8): (–)-(*S*)- **88c** t_R = 4.52 min and (+)-(*R*)- **88c** t_R = 4.95 min.

(*R*$_a$)-(1-(9H-Fluoren-1-yl)naphthalen-2-yl)trimethylsilane (88d)



Prepared according to general procedure **D** using methyl 9*H*-fluorene-1-carboxylate (44.9 mg, 200 µmol), chromatography with *n*-pentane to give a colorless gel (46.1 mg, 63%, e.r. 97:3 by HPLC): R_f 0.33 (*n*-pentane); $[\alpha]_D$ + 167.9 (c 0.50, $CHCl_3$); ν_{max} (neat): 3042w, 2954m, 2895w, 1588w, 1552w, 1501w, 14547w, 1402w, 1381w, 1308w, 1247m, 1148w, 1101w, 1023w, 979w, 909w, 877m, 834s, 812s, 755s, 706m, 686m, 624m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.89–7.95 (4H, m, C4*H*, C5*H*, C4'*H*, C5'*H*), 7.80 (1H, d, ^3J 8.4, C3*H*), 7.55 (1H, dd, ^3J 7.5, 7.5, C3'*H*), 7.49 (1H, dd, ^3J 8.2, 6.7, ^4J 1.3), 7.43 (1H, dd, ^3J 7.5), 7.36–7.40 (2H, m, C6*H*), 7.26–7.32 (3H, m, C7*H*, C2'*H*), 3.48 (1H, d, ^2J 22.3, C9'*H*), 3.42 (1H, d, ^2J 22.3, C9'H), 0.00 (9H, s, Si(C*H*$_3$)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.9 (*C1*), 143.3, 143.1, 141.5, 141.0, 138.2 (*C1'*), 135.6 (*C2*), 133.4 (*C4a*), 131.5 (*C8a*), 130.6 (*C3*), 129.1, 127.7, 126.7 (*C3*'), 126.55, 126.52, 126.4, 125.96, 125.93, 125.8, 124.8, 119.9, 119.2, 36.2 (*C9'*), 0.00 (Si(*C*H$_3$)$_3$); The e.r. was determined by HPLC using a Chiralcel OD-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (+)-(*R*)- **88d** t_R = 6.38 min and (–)-(*S*)- **88d** t_R = 7.88 min.

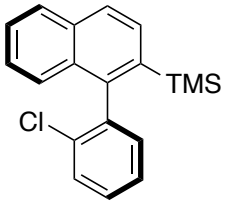
(*R*$_a$)-(1-(4'-Methyl-[1,1'-biphenyl]-2-yl)naphthalen-2-yl)trimethylsilane (88e)



Prepared according to general procedure **D** using methyl 4'-methyl-[1,1'-biphenyl]-2-carboxylate (45.3 mg, 200 µmol), chromatography with *n*-pentane:CH_2Cl_2 (95:5 to 90:10) to give a colorless gel (40.6 mg, 65%, e.r. 97:3 by HPLC): R_f 0.35 (*n*-pentane); $[\alpha]_D$ + 101.7 (c 0.50, $CHCl_3$); ν_{max} (neat): 3050w, 2952m, 2895w, 1551w, 1518w, 1480w, 1453w, 1406w, 1363w, 1311w, 1248m, 1166w, 1107w, 1025w, 967w, 866s, 814s, 755s, 689m, 647m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72–7.77 (2H, m, C4*H*), 7.59 (1H, d, ^3J 8.3, C3*H*), 7.48–7.53 (2H, m, C3'*H*, C4'*H*), 7.33–7.41 (3H, m, C6*H*, C5'*H*), 7.27–7.30 (1H, m, C6'*H*), 7.21–7.26 (1H, m), 6.92 (2H, d, ^3J 8.2, C2''*H*, C6''*H*), 6.77 (2H, d, ^3J 8.5, C3''*H*, C5''*H*), 2.12 (3H, s, C*H*$_3$), –0.07 (9H, s, Si(C*H*$_3$)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 145.7 (*C1*), 141.5 (*C2'*), 139.7 (*C1'*), 138.0 (*C1''*), 136.7 (*C2*), 136.0 (*C4''*), 133.1 (*C4a*), 132.6 (*C8a*), 132.1 (*C6'*), 130.5

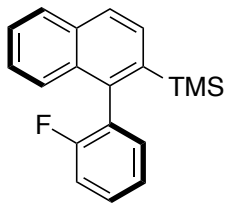
(*C3*), 130.0 (*C3'*), 128.9 (*C2''*, *C6''*), 128.2 (*C3''*, *C5''*), 128.1 (*C4'*), 127.6, 126.9, 126.5, 126.2 (*C4*), 125.8 (*C6*), 125.7, 20.9 (CH_3), 0.05 ($Si(CH_3)_3$); The e.r. was determined by HPLC using a Chiralcel OD-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (–)-(*S*)-**88e** t_R = 5.65 min and (+)-(*R*)-**88e** t_R = 7.62 min.

(R_a)-(1-(2-Chlorophenyl)naphthalen-2-yl)trimethylsilane (88f)



Prepared according to general procedure **D** using methyl 2-chlorobenzoate (34.1 mg, 200 µmol), reduction over Ti(O*i*-Pr)$_4$ for **1 h**, chromatography with *n*-pentane to give a colorless solid (40.6 mg, 65%, e.r. 98:2 by HPLC, m.p. 61.0–63.0 °C): R_f 0.35 (*n*-pentane); $[\alpha]_D$ + 62.6 (c 0.50, $CHCl_3$); ν_{max} (neat): 3059w, 2955m, 2898w, 1932w, 1549w, 1501w, 1473w, 1431m, 1362w, 1317w, 1248m, 1164w, 1124w, 1103w, 1056m, 1028w, 969w, 880m, 863m, 820s, 755s, 691m, 673m, 644m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83–7.89 (2H, m, C4*H*, C5*H*), 7.72 (1H, d, ^3J 8.3, C3*H*), 7.49–7.52 (1H, m, C3'*H*), 7.45 (1H, ddd, ^3J 8.1, 6.8, ^4J 1.3, C6*H*), 7.32–7.41 (3H, m, C7*H*, C4'*H*, C5'*H*), 7.29 (1H, dd, ^3J 7.0, ^4J 1.9, C6'*H*), 7.24 (1H, dd, ^3J 8.5, ^4J 1.0, C8*H*), 0.03 (9H, s, $Si(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.2 (*C1*), 139.7 (*C1'*), 135.9 (*C2*), 134.8 (*C2'*), 133.0 (*C4a*), 132.3 (*C6'*), 131.4 (*C8a*), 130.1 (*C3*), 128.9 (*C3'*), 128.7 (*C4'*), 127.4 (*C5*), 126.6 (*C4*), 125.9 (*C5'*), 125.74 (*C7*), 125.67 (*C6*), 125.4 (*C8*), –0.47 ($Si(CH_3)_3$); The e.r. was determined by HPLC using a Chiralpak AD-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (+)-(*R*)-**88f** t_R = 4.10 min and (–)-(*S*)-**88f** t_R = 4.48 min.

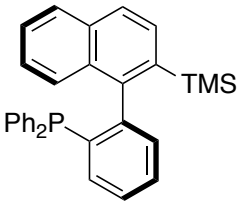
(R_a)-(1-(2-Fluorophenyl)naphthalen-2-yl)trimethylsilane (88g)



Prepared according to general procedure **D** using methyl 2-fluorobenzoate (30.8 mg, 200 µmol), chromatography with *n*-pentane to give a colorless solid (45.8 mg, 78%, e.r. 87:13 by HPLC, m.p. 76.9–78.9 °C): R_f 0.27 (*n*-pentane); $[\alpha]_D$ + 10.1 (c 0.50, $CHCl_3$); ν_{max} (neat): 3060w, 2955m, 2896w, 1930w, 1614w, 1582w, 1488m, 1447m, 1409w, 1360w, 1323w, 1247m, 1199w, 1168w, 1110w, 1093w, 1033w, 969w, 948w, 877m, 860s, 820s, 757s, 688m, 644m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83–7.89 (2H, m, C4*H*, C5*H*), 7.72 (1H, d, ^3J 8.3, C3*H*), 7.41–7.48 (2H, m), 7.32–7.37 (2H, m), 7.16–7.28 (3H, m), 0.04 (9H, s, $Si(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 161.7 (*C2'*), 159.7 (*C1'*), 140.1 (*C1*), 137.2 (*C2*), 133.5 (*C4a*), 133.2 (d, *J* 3.5), 132.5

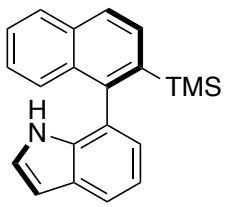
(*C8a*), 130.5 (*C3*), 129.8 (d, *J* 8.0), 128.8 (d, *J* 18), 127.9 (*C5*), 127.1 (*C4*), 126.2 (d, *J* 11.8), 125.9, 123.7 (d, *J* 3.6), 115.5 (d, *J* 22.0), 0.00 (Si(*C*H$_3$)$_3$); The e.r. was determined by HPLC using a Chiralpak IC-3 column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (+)-(*R*)-**88g** t_R = 4.18 min and (–)-(*S*)-**88g** t_R = 4.78 min.

(R_a)-Diphenyl(2-(2-(trimethylsilyl)naphthalen-1-yl)phenyl)phosphane (88h)



Prepared according to general procedure **D** using methyl 2-(diphenylphosphino)-benzoate (64.1 mg, 200 µmol) and (*S*,*Z*)-1-(2-Bromophenyl)-3-iodo-3-(trimethylsilyl)prop-2-en-1-ol (**99**) (164 mg, **400 µmol**), reduction over Ti(O*i*-Pr)$_4$ for **1 h**, chromatography with CH_2Cl_2:*n*-pentane (10:90 to 20:80) to give a colorless gel (58.1 mg, 63%, e.r. 95:5 by HPLC): R_f 0.24 (CH_2Cl_2:*n*-pentane 20:80); $[\alpha]_D$ + 71.2 (c 0.50, $CHCl_3$); ν_{max} (neat): 3051m, 2954m, 2895w, 1585w, 1553w, 1478w, 1434m, 1361w, 1309w, 1247m, 1185w, 1094w, 1026w, 999w, 966w, 908m, 867s, 836s, 814s, 759s, 735s, 693s, 646s; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.82 (1H, d, ^3J 8.3), 7.69–7.74 (2H, m), 7.38–7.46 (3H, m), 7.30–7.34 (1H, m), 7.23–7.27 (3H, m), 7.18–7.23 (3H, m), 7.12–7.16 (1H, m), 7.03–7.08 (2H, m), 6.93–6.98 (2H, m), 6.71–6.76 (2H, m), –0.01 (9H, s, Si(C*H*$_3$)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 147.7, 147.4, 145.6, 145.5, 139.0, 138.9, 137.9, 137.7, 136.7, 136.6, 136.09, 136.08, 134.3, 134.1, 133.82, 133.81, 133.6, 133.5, 132.9, 132.51, 132.49, 131.34, 131.30, 130.3, 128.5, 128.3, 128.24, 128.20, 128.1, 127.99, 127.93, 127.8, 127.2, 127.0, 126.7, 125.6, 124.8, 0.35 (Si(*C*H$_3$)$_3$); The e.r. was determined by HPLC using a Chiralpak IA column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (+)-(*R*)-**88h** t_R = 4.78 min and (–)-(*S*)-**88h** t_R = 5.42 min.

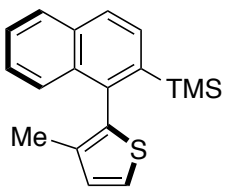
(S_a)-7-(2-(Trimethylsilyl)naphthalen-1-yl)-1H-indole (88i)



Prepared according to general procedure **D** using methyl 1 *H*-indole-7-carboxylate (35.0 mg, 200 µmol), which was deprotonated in a separate vessel in Et_2O (2 mL) at RT with *i*-PrMgCl (100 µL, 2.00 molL^{-1}, 200 µmol) and then added to the Grignard reagent. Chromatography with *n*-pentane:CH_2Cl_2 (90:10 to 80:20) to give a colorless gel (43.7 mg, 69%, e.r. 98:2 by HPLC): R_f 0.26 (*n*-pentane:CH_2Cl_2 90:10); $[\alpha]_D$ – 41.5 (c 0.50, $CHCl_3$); ν_{max} (neat): 3401s, 3051m, 2952m, 2895w, 1604w, 1549w, 1500w, 1485w, 1454w, 1427m, 1330m, 1247m, 1148w, 1097m, 1025m, 968w, 921w,

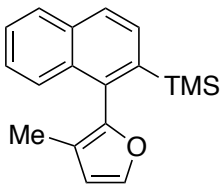
868s, 836s, 799s, 753m, 733s, 689m, 668m, 614m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.85–7.93 (2H, m, C4'*H*, C5'*H*), 7.77 (1H, d, ^{3}J 8.4, C3'*H*), 7.73 (1H, ddd, ^{3}J 8.0, ^{4}J 0.9, 0.9, C4*H*), 7.58 (1H, br, N*H*), 7.45 (1H, ddd, ^{3}J 8.2, 6.8, ^{4}J 1.3, C6'*H*), 7.34 (1H, dd, ^{3}J 8.5, ^{4}J 1.0, C8'*H*), 7.21–7.28 (2H, m, C5*H*, C7'*H*), 7.11 (1H, dd, ^{3}J 7.1, ^{4}J 1.0, C6*H*), 7.04–7.06 (1H, m, C2*H*), 6.59–6.63 (1H, m, C3*H*), –0.16 (9H, s, Si(CH_3)); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.7 (*C1'*), 137.8 (*C2'*), 136.0 (*C7a*), 133.7 (*C4a'*), 132.4 (*C8a'*), 130.9 (*C3'*), 127.8 (*C5'*), 127.4 (*C3a*), 127.0 (*C4'*), 126.4 (*C8'*), 126.3 (*C6'*), 126.1 (*C7'*), 124.7 (*C7*), 124.3 (*C6*), 124.1 (*C2*), 120.2 (*C4*), 119.6 (*C5*), 102.6 (*C3*), –0.07 (Si(*C*H_3)$_3$); The e.r. was determined by HPLC using a Chiralpak IA column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (–)-(*R*)-**88i** t_R = 8.28 min and (+)-(*S*)-**88i** t_R = 9.20 min. ESI-MS: m/z calcd. for $C_{21}H_{22}NSi$ 316.1516 found 316.1516 [$MH^{\cdot+}$].

(*S*$_a$)-(1-(3-Methylthiophen-2-yl)naphthalen-2-yl)trimethylsilane (88j)



Prepared according to general procedure **D** using methyl 3-methylthiophene-2-carboxylate (31.2 mg, 200 µmol), chromatography with *n*-pentane to give a colorless gel (46.0 mg, 78%, e.r. 95:5 by HPLC): R_f 0.43 (*n*-pentane); $[\alpha]_D$ + 10.6 (c 0.50, $CHCl_3$); ν_{max} (neat): 3051w, 2952m, 2895w, 1557w, 1500w, 1453w, 1407w, 1346w, 1315w, 1247m, 1166w, 1098w, 1025w, 928w, 866s, 830s, 815s, 757s, 709s, 664m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.86–7.92 (2H, m, C4*H*, C8*H*), 7.74 (1H, d, ^{3}J 8.3, C3*H*), 7.47–7.53 (2H, m), 7.40–7.45 (1H, m), 7.37 (1H, d, ^{3}J 5.1, C5'*H*), 7.02 (1H, d, ^{3}J 5.1, C4'*H*), 1.95 (3H, s, CH_3), 0.19 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.8 (*C1*), 138.1 (*C2*), 136.6 (*C2'*), 136.3 (*C3'*), 133.8, 133.7, 130.6 (*C3*), 129.4 (*C4'*), 128.0, 127.7, 126.5, 126.4, 126.3, 124.2 (*C5'*), 14.5 (*C*H_3), 0.19 (Si(*C*H_3)$_3$); The e.r. was determined by HPLC using a Chiralcel OJ-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (–)-(*R*)-**88j** t_R = 4.73 min and (+)-(*S*)-**88j** t_R = 7.85 min.

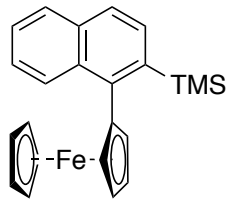
(1-(3-Methylfuran-2-yl)naphthalen-2-yl)trimethylsilane (88k)



Prepared according to general procedure **D** using methyl 3-methylfuran-2-carboxylate (28.0 mg, 200 µmol), chromatography with *n*-pentane to give a colorless gel (28.0 mg, 50%): R_f 0.29 (*n*-pentane); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (1H, d, ^{3}J 8.2, C4*H*), 7.84 (1H, d, ^{3}J 8.0, C5*H*), 7.72 (1H, d, ^{3}J 8.3, C3*H*), 7.48–7.53 (2H, m, C5'*H*, C8*H*), 7.46 (1H, ddd, ^{3}J 8.1, 6.7, ^{4}J 1.4,

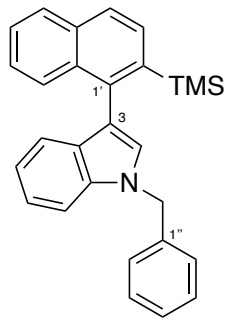
C6*H*), 7.41 (1H, ddd, ^{3}J 8.3, 6.8, ^{4}J 1.5, C7*H*), 6.43 (1H, d, ^{3}J 1.8, C4'*H*), 1.83 (3H, s, CH_3), 0.11 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.4 (*C2'*), 141.0 (*C8*), 140.7 (*C2*), 134.8 (*C1*), 133.6 (*C4a*), 133.3 (*C8a*), 130.5 (*C3*), 128.0 (*C4*), 127.9 (*C5*), 126.4 (*C7*), 126.2 (*C6*), 125.8 (*C5'*), 118.8 (*C3'*), 113.3 (*C4'*), 10.5 (*C*H_3), –0.65 (Si(*C*H_3)$_3$).

(2-(Trimethylsilyl)naphthalen-1-yl)-ferrocene (88l)



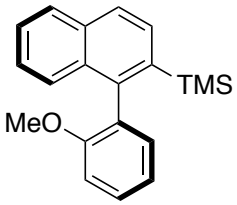
Prepared according to general procedure **D** using methyl ferrocenecarboxylate (48.8 mg, 200 µmol), chromatography with *n*-pentane:CH_2Cl_2 (98:2 to 95:5) to give an orange/red solid (44.0 mg, 57%): R_f 0.34 (*n*-pentane:CH_2Cl_2 95:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.94 (1H, dd, ^{3}J 8.7, ^{4}J 1.0, C8'*H*), 7.86 (1H, dd, ^{3}J 8.0, ^{4}J 1.3, C5'*H*), 7.78 (1H, d, ^{3}J 8.3, C4'*H*), 7.60–7.64 (2H, m, C3'*H*, C7'*H*), 7.53 (1H, ddd, ^{3}J 7.45, 7.45, ^{4}J 1.2, C6'*H*), 4.66 (2H, dd, ^{3}J 1.8, ^{4}J 1.8, C2*H*, C5*H*), 4.47 (2H, dd, ^{3}J 1.9, 1.9, C3*H*, C4*H*), 4.19 (5H, s, Cp–*H*), 0.12 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.0 (*C1'*), 139.7 (*C2'*), 133.8 (*C4a'*), 131.8 (*C8a'*), 131.5 (*C3'*), 127.8 (*C5'*), 127.7 (*C8'*), 126.0 (*C4'*), 125.9 (*C6'*), 124.0 (*C7'*), 90.5 (*C1*), 72.3 (*C2*, *C5*), 69.6 (*Cp*), 67.9 (*C3*, *C4*), 1.8 (Si*C*H_3)$_3$).

1-Benzyl-3-(2-(trimethylsilyl)naphthalen-1-yl)-1H-indole (88m)



Prepared according to general procedure **D** using methyl 1-benzylindole-3-carboxylate (53.1 mg, 200 µmol), chromatography with *n*-pentane: CH_2Cl_2 (90:10 to 80:20) to give a colorless gel (45.7 mg, 84%): R_f 0.35 (*n*-pentane:CH_2Cl_2 80:20); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83–7.87 (2H, m, C4'*H*, C5'*H*), 7.72 (1H, d, ^{3}J 8.3, C3'*H*), 7.57 (1H, c, ^{3}J 8.4, C8'*H*), 7.39–7.45 (2H, m, C7*H*, C6'*H*), 7.30–7.35 (2H, m, C3''*H*, C5''*H*), 7.20–7.30 (5H, m, C6*H*, C7'*H*, C2''*H*, C4''*H* C6''*H*), 7.13 (1H, ddd, ^{3}J 7.2, ^{4}J 1.0, ^{5}J 1.0, C4*H*), 7.07 (1H, s, C2*H*), 7.02 (1H, ddd, ^{3}J 6.9, 6.9, ^{4}J 1.0, C5*H*), 5.45 (1H, ^{2}J 15.7, CH_2), 5.35 (1H, ^{2}J 15.7, CH_2), –0.08 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.4 (*C1'*), 138.8 (*C2'*), 137.4 (*C1''*), 135.9 (*C7a*), 134.0 (*C8a'*), 133.6 (*C4a'*), 130.7 (*C3'*), 130.2 (*C3a*), 128.8 (*C3''*, *C5''*), 128.2 (*C2*), 127.8 (*C5'*), 127.7 (*C4''*), 127.2 (*C2''*, *C6''*), 127.0 (*C8'*), 126.5 (*C4'*), 126.0 (*C6'*), 125.6 (*C7'*), 122.0 (*C6*), 120.8 (*C4*), 119.7 (*C5*), 116.3 (*C3*), 109.6 (*C7*), 50.2 (*C*H_2), 0.51 (Si(*C*H_3)$_3$).

(R_a)-(1-(2-Methoxyphenyl)naphthalen-2-yl)trimethylsilane (88n) (absolute configuration assigned by analogy)



Prepared according to general procedure **D** using methyl 2-methoxybenzoate (33.2 mg, 200 µmol), reduction with modified reduction procedures:

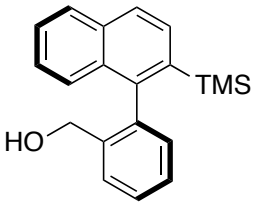
Reduction with $TiCl_4$:

Addition of THF (4.0 mL), $TiCl_4$ (110 µL, 1.00 mmol) and pyridine (161 µL, 2.00 mmol) and stirred at 60 °C for 2 h. Workup as described in general procedure A. Chromatography with *n*-pentane:CH_2Cl_2 (100:0 to 85:15) to give a colorless oil (44.7 mg, 73%, e.r. 68:32 by HPLC)

Reduction with PPh_3, I_2:

Addition of Amberlite IRC86 H-Form wet (300 mg), filtration of reaction mixture through pipette with cotton wool filter, purge with Et_2O (4 x 1.0 mL). Addition of a solution of PPh_3 (157 mg, 600 µmol) in Et_2O (2.0 mL) followed by the addition of a solution of iodine (152 mg, 600 µmol) in Et_2O (5 mL). The mixture was stirred for 30 min at RT. Workup with aq. halfsat. $NaHCO_3$-solution (10 mL) and Na_2SO_3 (few drops, until decolorization), extraction with Et_2O, dry over Na_2SO_4. Chromatography with *n*-pentane:CH_2Cl_2 (100:0 to 85:15) to give a colorless oil (29.8 mg, 49%, e.r. 91:9 by HPLC): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.81–7.85 (2H, m, C4*H*, C5*H*), 7.71 (1H, d, ^3J 8.3, C3*H*), 7.41–7.46 (2H, m, C6*H*, C4'*H*), 7.28–7.35 (2H, m, C7*H*, C8*H*), 7.14 (1H, dd, ^3J 7.3, ^4J 1.8, C6'*H*), 7.05 (1H, ddd, ^3J 7.4, 7.4, ^4J 1.1, C5'*H*), 6.99 (1H, dd, ^3J 8.3, ^4J 0.9, C3'*H*), 3.64 (3H, s, CH_3), 0.00 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 157.9 (*C2'*), 143.5 (*C1*), 136.4 (*C2*), 133.4 (*C4a*), 132.6 (*C6'*), 132.5 (*C8a*), 130.6 (*C3*), 130.0 (*C1'*), 129.2 (*C4'*), 127.7 (*C5*), 126.4 (*C2*), 126.37 (*C8*), 125.9 (*C6*), 125.6 (*C7*), 120.0 (*C5'*), 110.3 (*C3'*), 55.1 (*C*H_3), –0.01 (Si(*C*H_3)$_3$); The e.r. was determined by HPLC using a Chiralpak IA column (0.50 mLmin^{-1}, *i*-PrOH:*n*-heptane 1:99): (*R*)- **88n** t_R = 7.70 min and (*S*)- **88n** t_R = 8.07 min.

(*R_a*)-(2-(2-(trimethylsilyl)naphthalen-1-yl)phenyl)methanol (88o) (absolute configuration assigned by analogy)



Prepared according to general procedure **D** using methyl phthalide (26.8 mg, 200 µmol), reduction with Ti(O*i*-Pr)$_4$ according to procedure **D** gave a colorless oil (25.6 mg, 42%, e.r. 85:15 by HPLC).

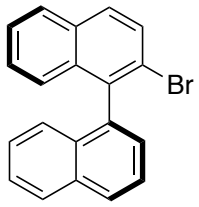
With modified reduction procedures:

Reduction with $TiCl_4$:

Addition of THF (4.0 mL), $TiCl_4$ (110 µL, 1.00 mmol) and pyridine (161 µL, 2.00 mmol) and stirred at 60 °C for 2 h. Workup as described in general procedure A. Chromatography with *n*-pentane:CH_2Cl_2 (50:50) to give a colorless oil (37.1 mg, 61%, e.r. 88:12 by HPLC): ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.74–7.82 (2H, m), 7.64 (1H, d, ^3J 8.5, C3'*H*), 7.52–7.59 (1H, m), 7.11–7.47 (6H, m), 4.05–4.26 (2H, m, CH_2), 1.29 (1H, t, ^3J 6.2, O*H*), –0.09 (Si(CH_3)$_3$). The e.r. was determined by HPLC using a Chiralpak IA column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 5:95): (*R*)-**88o** t_R = 7.87 min and (*S*)-**88o** t_R = 8.28 min.

C. Derivatization

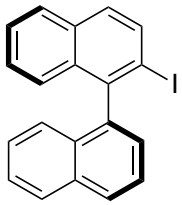
(*R_a*)-2-Bromo-1,1'-binaphthalene (113a)



A solution of (*R*)-[1,1'-Binaphthalen]-2-yltrimethylsilane (65.3 mg, 200 µmol) and N-bromosuccinimide (142 mg, 800 µmol) in MeCN (6.0 mL) was stirred at 50 °C for 24 h. The solvent was evaporated *in vacuo*. Purification by chromatography *n*-pentane:CH_2Cl_2 (100:0 to 95:5) to give a white solid (53.1 mg, 80%, e.r. 98:2 by HPLC, m.p. 121.4–123.5 °C): R_f 0.24 (pentane); $[\alpha]_D$ – 8.65 (c 1.00, $CHCl_3$); ν_{max} (neat): 3054m, 1616w, 1580m, 1503m, 1424w, 1372m, 1311w, 1273w, 1256w, 1212w, 1160w, 1134w, 1114m, 1069w,1041w, 1015w, 944w, 907m, 865w, 834m, 802s, 774s, 730s, 685m, 665m, 624m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99 (1H, d, ^3J 8.3, C4'*H*), 7.95 (1H, d, ^3J 8.2, C5'*H*), 7.89 (1H, d, ^3J 8.2, C5*H*), 7.77–7.84 (2H, m, C3*H*, C4*H*), 7.62 (1H, dd, ^3J 7.0, 8.3, C3'*H*), 7.44–7.50 (2H, m, C6*H*, C6'*H*), 7.40 (1H, dd, ^3J 7.0, ^4J 1.2, C2'*H*), 7.24–7.32 (2H, m, C7*H*, C7'*H*), 7.20–7.23 (1H, m, C8'*H*), 7.18 (1H, m, C8*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.1 (*C1*), 137.3 (*C1'*), 134.4 (*C8a*), 133.6 (*C4a'*), 132.3 (*C4a*), 132.0 (*C8a'*), 130.0 (*C3*), 129.3 (*C4*), 128.3 (*C4'*, *C5'*), 127.95 (*C5*), 127.92 (*C2'*), 126.9 (*C7*), 126.8 (*C8*),

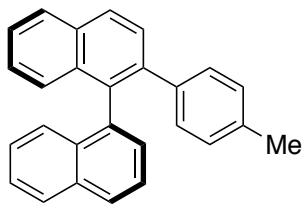
126.3 (*C7'*), 126.1 (*C6*), 126.0 (*C6'*), 125.7 (*C8'*), 125.5 (*C3'*), 122.7 (*C2*); The e.r. was determined by HPLC using a Chiralcel OJ-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 5:95): (+)-(*S*)-**113a** t_R = 7.72 min and (–)-(*R*)-**113a** t_R = 12.75 min.

(*R*$_a$)-2-Iodo-1,1'-binaphthalene (114a)



To a solution of (*R*)-[1,1'-Binaphthalen]-2-yltrimethylsilane (65.3 mg, 200 µmol) in CH_2Cl_2 (2.0 mL) at 0 °C was added a solution of ICl (64.9 mg, 400 µmol) in CH_2Cl_2 (2.0 mL) dropwise over 5 min. The mixture was allowed to warm to RT and stirred for 30 min. CH_2Cl_2 (20 mL), H_2O (9.0 mL) and an aqueous saturated Na_2SO_3 solution (1.0 mL) were added. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL), the combined organics were dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. Purification by chromatography (*n*-pentane:CH_2Cl_2 98:2) gave a white solid (65.2 mg, 86%, e.r. 98:2 by HPLC, m.p. 129.0–130.5 °C): R_f 0.24 (pentane); $[\alpha]_D$ – 22.6 (c 1.00, $CHCl_3$); ν_{max} (neat): 3043m, 1815w, 1614w, 1578m, 1562w, 1501m, 1418w, 1369m, 1309w, 1256m, 1211w, 1159w, 1132w, 1103m, 1068w, 1040w, 1013w, 959w, 908w, 862w, 800s, 773s, 743s, 684m, 664m, 622m; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.04 (1H, d, ^3J 8.7, C3*H*), 8.00 (1H, d, ^3J 8.3, C4'*H*), 7.96 (1H, d, ^3J 8.2, C5'*H*), 7.89 (1H, d, ^3J 8.2, C5*H*), 7.67 (1H, d, ^3J 8.7, C4*H*), 7.63 (1H, dd, ^3J 8.3, 7.0, C6*H*), 7.45–7.51 (2H, m, C6*H*, C6'*H*), 7.36 (1H, dd, ^3J 7.0, ^4J 1.2, C2'*H*), 7.28–7.33 (1H, m, C7'*H*), 7.21–7.25 (1H, m, C7*H*), 7.16–7.21 (2H, m, C8*H*, C8'*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.8 (C1), 140.9 (C1'), 135.6 (C3), 134.0 (C8a), 133.7 (C4a'), 132.8 (C4a), 131.8 (C8a'), 129.2 (C4), 128.4 (C4'), 128.3 (C5'), 127.9 (C5, C2'), 127.3 (C8), 126.9 (C7), 126.4 (C7'), 126.3 (C6), 126.0 (C6'), 125.7 (C8'), 125.5 (C3'), 99.6 (C2); The e.r. was determined by HPLC using a Chiralcel OJ-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 5:95): (+)-(*S*)-**114a** t_R = 7.63 min and (–)-(*R*)-**114a** t_R = 11.65 min.

(*R*$_a$)-2-(*p*-Tolyl)-1,1'-binaphthalene (116a)

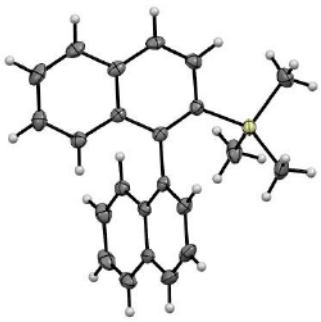


To a solution of (*R*)-[1,1'-Binaphthalen]-2-yltrimethylsilane (65.3 mg, 200 µmol) in *n*-heptane (2.0 mL) at 0 °C was added a solution of ICl (64.9 mg, 400 µmol) in *n*-heptane (2.0 mL) dropwise over 5 min and the mixture was stirred at 0 °C for 30 min. THF

(0.5 mL), a solution of 4-Methylphenylzinc chloride in THF (2.00 mL, 0.40 molL^{-1}, 800 µmol) and a solution $Pd(PPh_3)_4$ (11.6 mg, 10.0 µmol) in THF (2.0 mL) was added. The mixture was allowed to warm to RT and stirred for 2.5 h at RT. The mixture was cooled to 0 °C, Et_2O (15 mL) and an aqueous HCl-solution (1 molL^{-1}, 20 mL) were added. The phases were separated and the aqueous phase was extracted with Et_2O (2 x 15 mL), the combined organics were dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. Purification by chromatography (*n*-pentane:CH_2Cl_2 95:5) gave a colorless gel (49,6 mg, 72%, e.r. 98:2 by HPLC): R_f 0.15 (*n*-pentane:CH_2Cl_2 95:5); $[\alpha]_D$ −177.1 (c 1.00, $CHCl_3$); ν_{max} (neat): 3051m, 2919w, 2864w, 2341w, 1907w, 1813w, 1619w, 1593w, 1503m, 1452w, 1366m, 1336w, 1257w, 1212w, 1185w, 1112w, 1021m, 946w, 907m, 864w, 830w, 804s, 779s, 749s, 694m, 646w, 618w; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.97 (1H, d, ^3J 8.5, C4*H*), 7.91 (1H, d, ^3J 8.2, C5*H*), 7.83 (1H, d, ^3J 8.2, C5'*H*) 7.78 (1H, d, ^3J 8.3, C4'*H*), 7.64 (1H, d, ^3J 8.5, C3*H*), 7.34–7.44 (4H, m, C6*H*, C3'*H*, C7'*H*), 7.18–7.26 (4H, m, C2'*H*), 6.96 (2H, d, ^3J 8.1, C2''*H*, C6''*H*), 6.80 (2H, d, ^3J 7.9, C3''*H*, C5''*H*), 2.14 (3H, s, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.4 (*C2*), 139.0 (*C1''*), 137.1 (*C1'*), 135.8 (*C4''*), 135.5 (*C1*), 133.6 (*C8a'*), 133.3 (*C8a*), 133.2 (*C4a'*), 132.5 (*C4a*), 129.1 (*C2'*), 129.0 (*C2''*, *C6''*), 128.5 (*C3*), 128.2 (*C3''*, *C5''*), 128.15 (C5'), 127.9 (*C4*), 127.8 (*C5*), 127.4 (*C4'*), 127.1, 126.6, 126.2, 126.0 (*C7'*), 125.6, 125.5, 125.3, 21.0 (CH_3); Chiralpak AD-H column (1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (−)-(*R*)-**116a** t_R = 7.55 min and (+)-(*S*)-**116a** t_R = 10.08 min.

X-ray Data

Crystal data for (*R*)-[1,1'-binaphthalen]-2-yltrimethylsilane

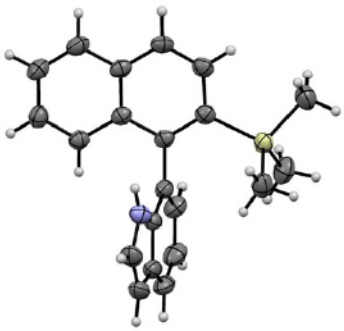


The crystal was measured on a *Bruker Kappa Apex2* diffractometer at 123K using graphite-monochromated Cu K_α-radiation with λ = 1.54178 Å, Θ_{max} = 70.443°. Minimal/maximal transmission 0.89/0.91, µ = 1.105 mm^{-1}. The Apex2 suite has been used for data collection and integration. From a total of 96941 reflections, 6920 were independent (merging r = 0.032). From these, 6822 were considered as observed (I>2.0σ(I)) and were used to refine 434 parameters. The structure was solved by Other methods using the program Superflip. Least-squares refinement against F was

carried out on all non-hydrogen atoms using the program CRYSTALS. R = 0.0270 (observed data), wR = 0.0310 (all data), GOF = 1.0762. Minimal/maximal residual electron density = –0.19/0.29 e Å^{-3}. Chebychev polynomial weights were used to complete the refinement.

Chemical formula	$C_{23}H_{22}Si$
Formula weight	326.51
Z	8
$D_{calc.}$	1.186 Mg m^{-3}
F(000)	1392
Crystal description	colorless block
Crystal size	0.090 0.110 0.140 mm^3
Absorption coefficient	1.105 mm^{-1}
min/max transmission	0.89 / 0.91
Temperature	123K
Radiation (wavelength)	Cu K_α (λ = 1.54178 Å)
Crystal system	orthorhombic
Space group	P 2_1 2_1 2_1
Unit cell dimensions	a = 9.3290(10) Å b = 19.488(2) Å c = 20.124(2) Å α = 90° β = 90° γ = 90°
Volume	3658.6(7) Å^3
min/max Θ	4.394° / 70.443°
Number of collected reflections	96941
Number of independent reflections	6920 (merging r = 0.032)
Number of observed reflections	6822 (I>2.0σ(I))
Number of refined parameters	434
R	0.0270
wR	0.0310
Goodness of fit	1.0762
Flack	0.026(13)

Crystal data for (*S*)-7-(2-(trimethylsilyl)naphthalen-1-yl)-1H-indole

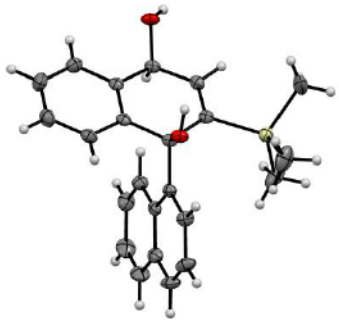


The crystal was measured on a *Stoe StadiVari* diffractometer at 123K using graphite-monochromated Ga K_α-radiation with λ = 1.34143 Å, Θ_{max} = 59.365°. Minimal/maximal transmission 0.96/0.98, μ = 0.752 mm^{-1}. The Apex2 suite has been used for data collection and integration. From a total of 164709 reflections, 7606 were independent (merging r = 0.052). From these, 7348 were considered as observed (I>2.0σ(I)) and were used to refine

424 parameters. The structure was solved by Other methods using the program SIR92. Least-squares refinement against F was carried out on all non-hydrogen atoms using the program CRYSTALS. R = 0.0358 (observed data), wR = 0.0417 (all data), GOF = 1.0866. Minimal/maximal residual electron density = –0.25/0.24 e $Å^{-3}$. Chebychev polynomial weights were used to complete the refinement.

Chemical formula	$C_{21}H_{21}NSi$
Formula weight	315.49
Z	4
$D_{calc.}$	1.205 Mg m^{-3}
F(000)	1344
Crystal description	colorless block
Crystal size	0.030 0.050 0.150 mm^3
Absorption coefficient	0.752 mm^{-1}
min/max transmission	0.96 / 0.98
Temperature	123K
Radiation (wavelength)	Ga K_α (λ = 1.34143 Å)
Crystal system	orthorhombic
Space group	P 2_1 2_1 2_1
Unit cell dimensions	a = 8.87000(10) Å b = 19.5663(2) Å c = 20.0422(2) Å α = 90° β = 90° γ = 90°
Volume	3478.39(6) $Å^3$
min/max Θ	2.746° / 59.365°
Number of collected reflections	164709
Number of independent reflections	7606 (merging r = 0.052)
Number of observed reflections	7348 (I>2.0σ(I))
Number of refined parameters	424
R	0.0358
wR	0.0417
Goodness of fit	1.0866
Flack	0.02 (2)

Crystal data for (1S,4S)-2-(trimethylsilyl)-[1,1'-binaphthalene]-1,4(4H)-diol



The crystal was measured on a *Bruker Kappa Apex2* diffractometer at 123K using graphite-monochromated Cu K_α-radiation with λ = 1.54178 Å, Θ_{max} = 68.966°. Minimal/maximal transmission 0.89/0.94, μ = 1.164 mm^{-1}. The Apex2 suite has been used for data collection and integration. From a total of 25978 reflections, 3593 were independent (merging r = 0.027). From these, 3533 were considered as observed (I>2.0σ(I)) and were used to refine 244 parameters. The structure was solved by Other methods using the program Superflip. Least-squares refinement against F was carried out on all non-hydrogen atoms using the program CRYSTALS. R = 0.0248 (observed data), wR = 0.0282 (all data), GOF = 1.0903. Minimal/maximal residual electron density = –0.18/0.27 e $Å^{-3}$. Chebychev polynomial weights were used to complete the refinement.

Chemical formula	$C_{23}H_{24}O_2Si$
Formula weight	360.53
Z	4
$D_{calc.}$	1.231 Mg m^{-3}
F(000)	768
Crystal description	colorless needle
Crystal size	0.050 0.100 0.210 mm^3
Absorption coefficient	1.164 mm^{-1}
min/max transmission	0.89 / 0.94
Temperature	123K
Radiation (wavelength)	Cu K_α (λ = 1.54178 Å)
Crystal system	orthorhombic
Space group	P 2_1 2_1 2_1
Unit cell dimensions	a = 7.2791(6) Å b = 13.3662(11) Å c = 19.9984(16) Å α = 90° β = 90° γ = 90°
Volume	1945.7(3) $Å^3$
min/max Θ	3.978° / 68.966°
Number of collected reflections	25978
Number of independent reflections	3593 (merging r = 0.027)
Number of observed reflections	3533 (I>2.0σ(I))
Number of refined parameters	244
R	0.0248
wR	0.0282
Goodness of fit	1.0903
Flack	0.024(18)

D. Determination of the Bond Rotational Barrier

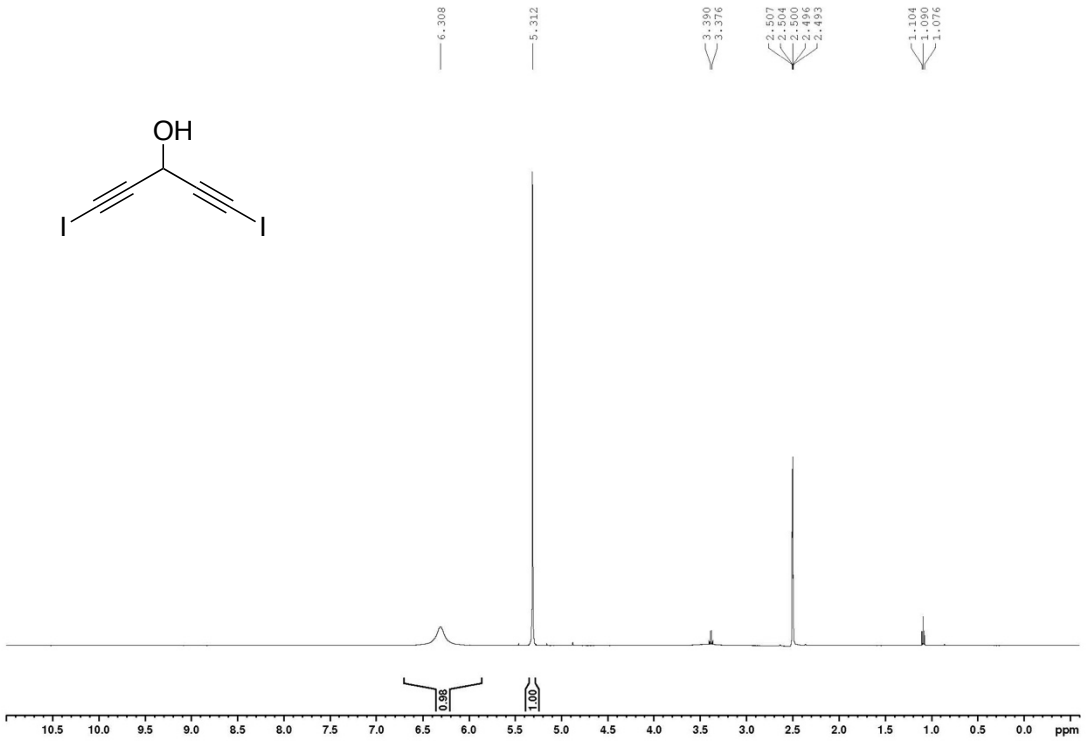
(*R*)-(1-(2-Fluorophenyl)naphthalen-2-yl)trimethylsilane (2 mg) in *n*-heptane (1.5 mL) was heated to 60 °C. After specified times aliquots (0.10 mL) were cooled to RT, diluted in *n*-heptane (1.0 mL) and the enantiomeric ratio (e.r.) was determined by HPLC using a Chiralpak IC-3 column ((1.00 mLmin^{-1}, i-PrOH:*n*-heptane 0.2:99.8): (+)-(*R*)-9 t_R = 4.18 min and (–)-(*S*)-9 t_R = 4.78 min). The rate constant of racemization (k_{rac}) and the Gibbs free energy $\Delta G^{\ddagger}$ were calculated according to the procedure described in literature (with k_e = ½ k_{rac}).[113]

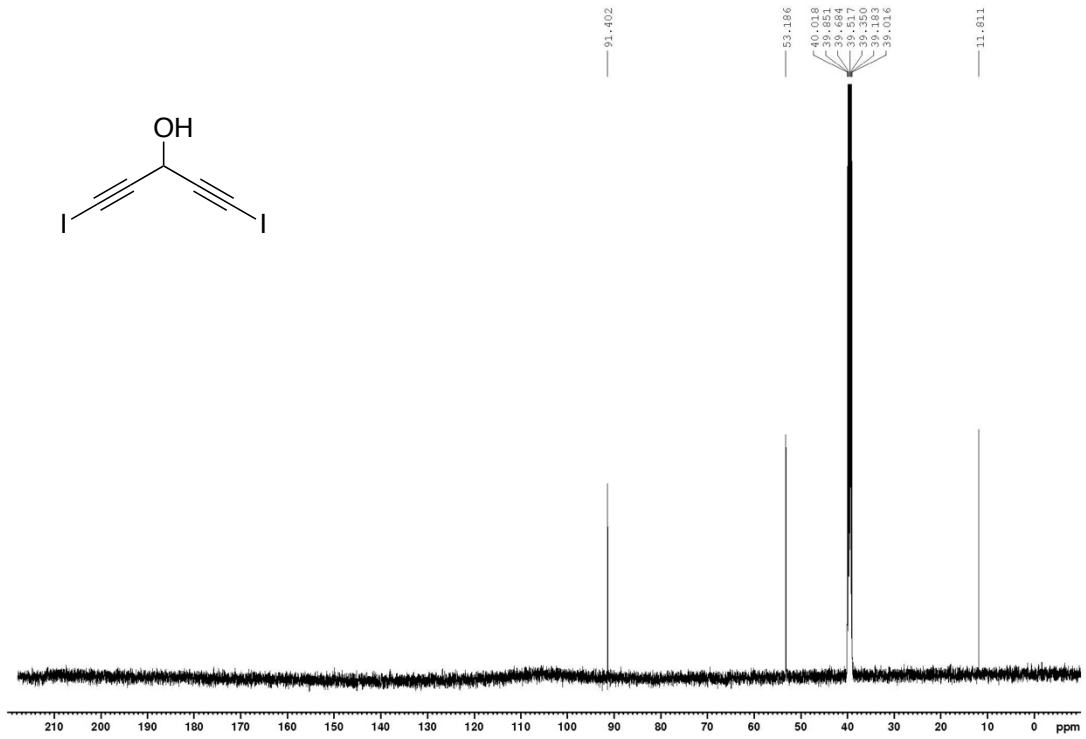
T= 60.0 °C, k_{rac} = 2.131•10^{-5} s^{-1}, $\Delta G^{\ddagger}$ **= 111.6 kJmol^{-1}**.

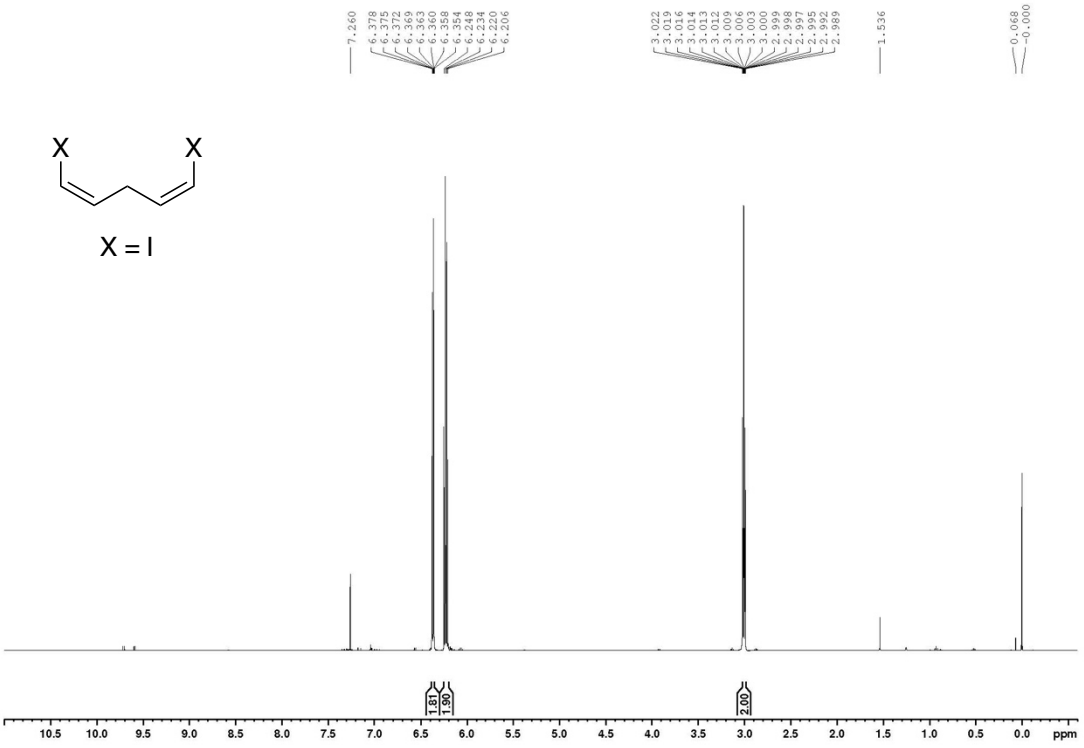
(*S*)-(1-(3-Methylthiophen-2-yl)naphthalen-2-yl)trimethylsilane (2 mg) in *n*-heptane (1.5 mL) was heated to 60 °C. After specified times aliquots (0.10 mL) were cooled to RT, diluted in *n*-heptane (1.0 mL) and the enantiomeric ratio (e.r.) was determined by HPLC using a Chiralcel OJ-H column ((1.00 mLmin^{-1}, *i*-PrOH:*n*-heptane 0.2:99.8): (–)-(*R*)-**9** t_R = 4.73 min and (+)-(*S*)-**9** t_R = 7.85 min). The rate constant of racemization (k_{rac}) and the Gibbs free energy $\Delta G^{\ddagger}$ were calculated according to the procedure described in literature (with k_e = ½ k_{rac}).[113]

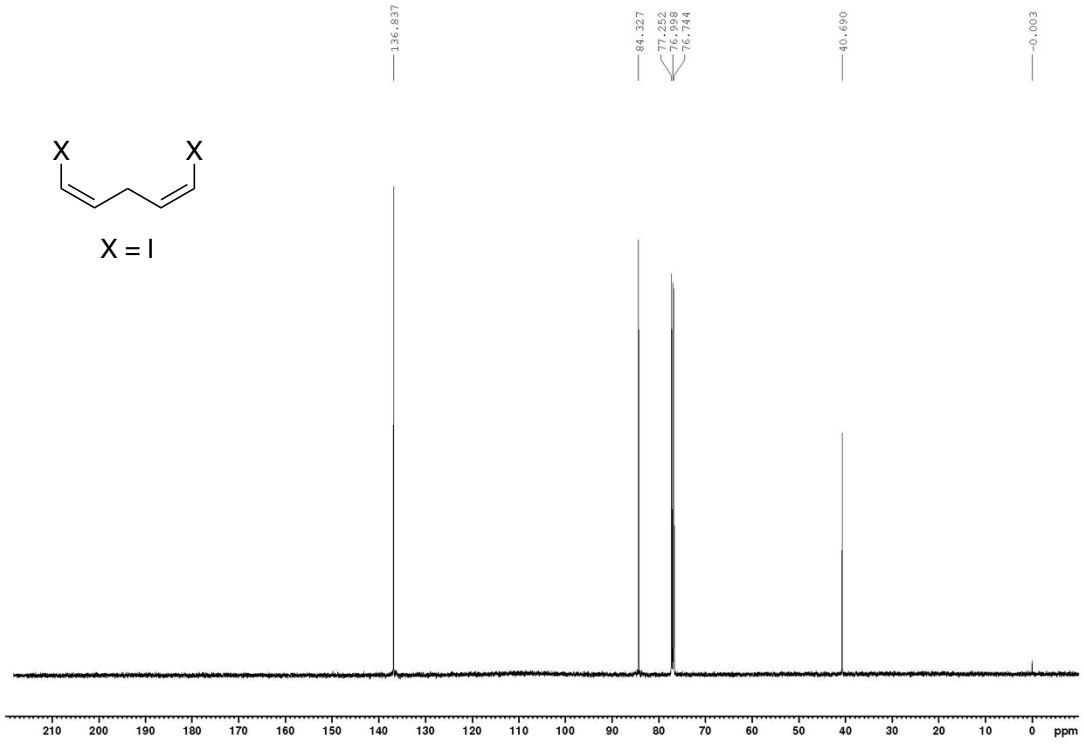
T= 60.0 °C, k_{rac} = 4.529•10^{-6} s^{-1}, $\Delta G^{\ddagger}$ **= 115.9 kJmol^{-1}**.

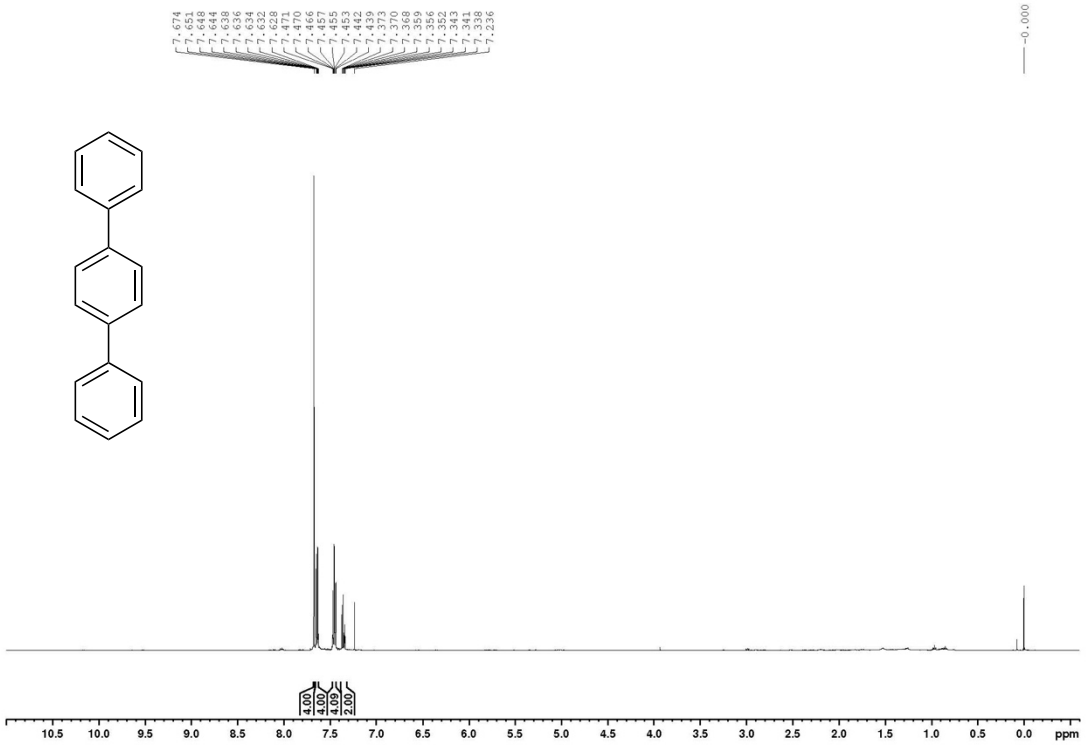
NMR Data

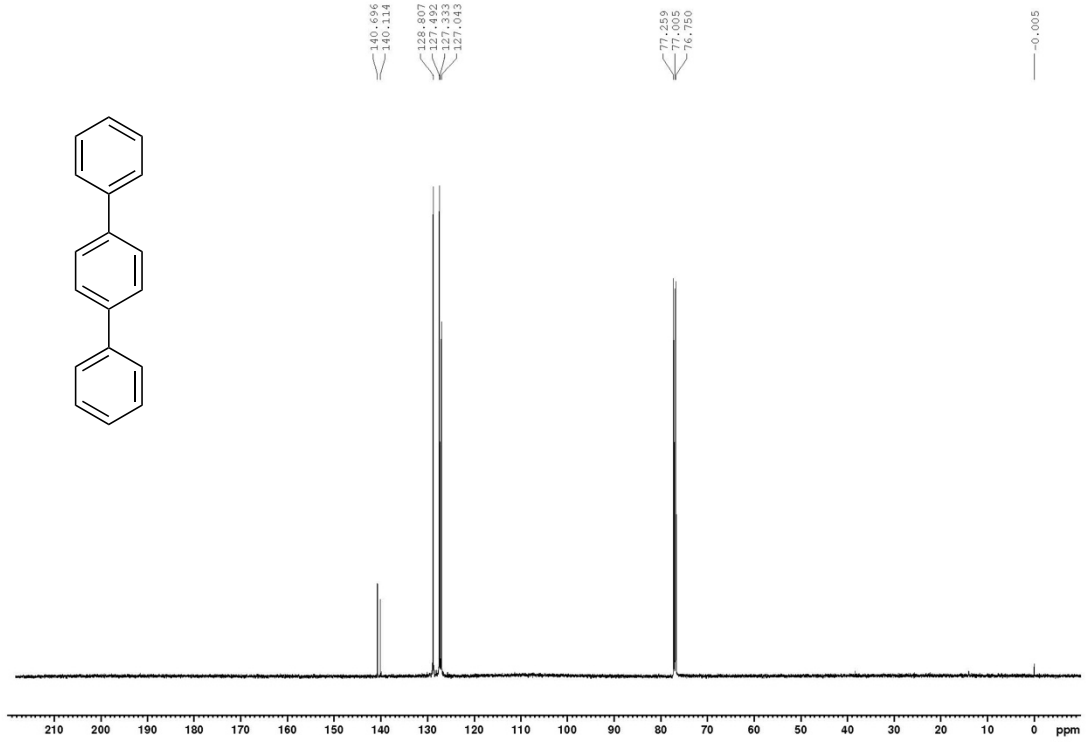

6.308
5.312
3.390
3.376
2.507
2.504
2.500
2.496
2.493
1.104
1.090
1.076
OH
I
I
0.98
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

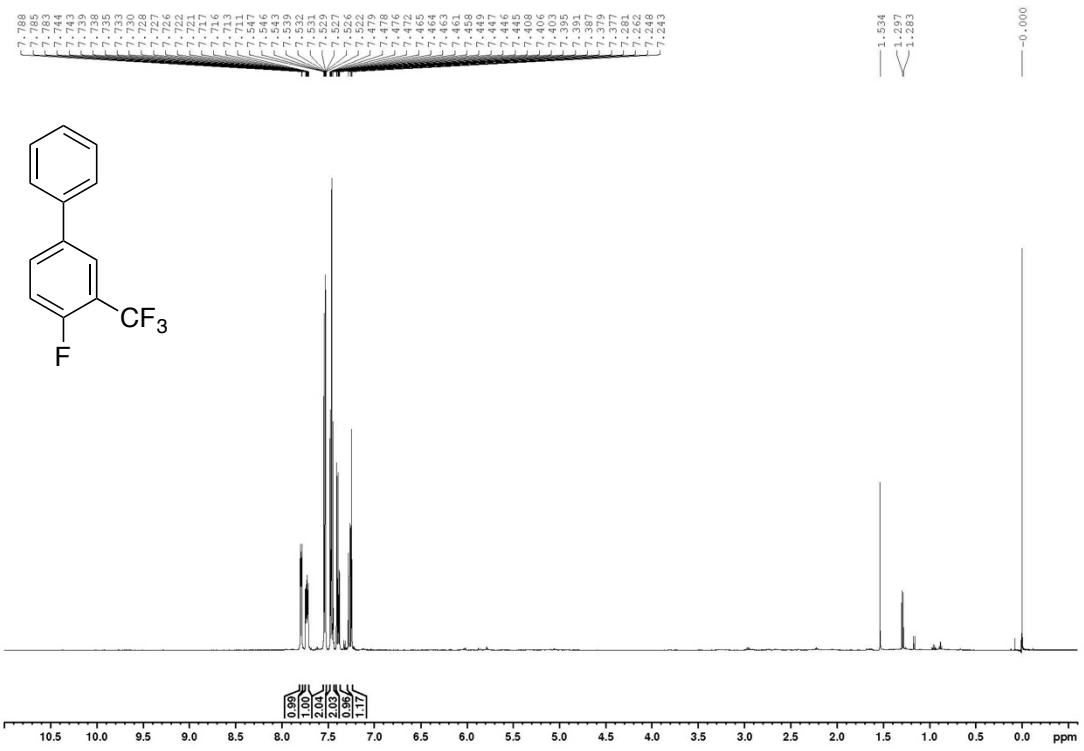

91.402
53.186
40.018
39.851
39.684
39.517
39.350
39.183
39.016
11.811
OH
I
I
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

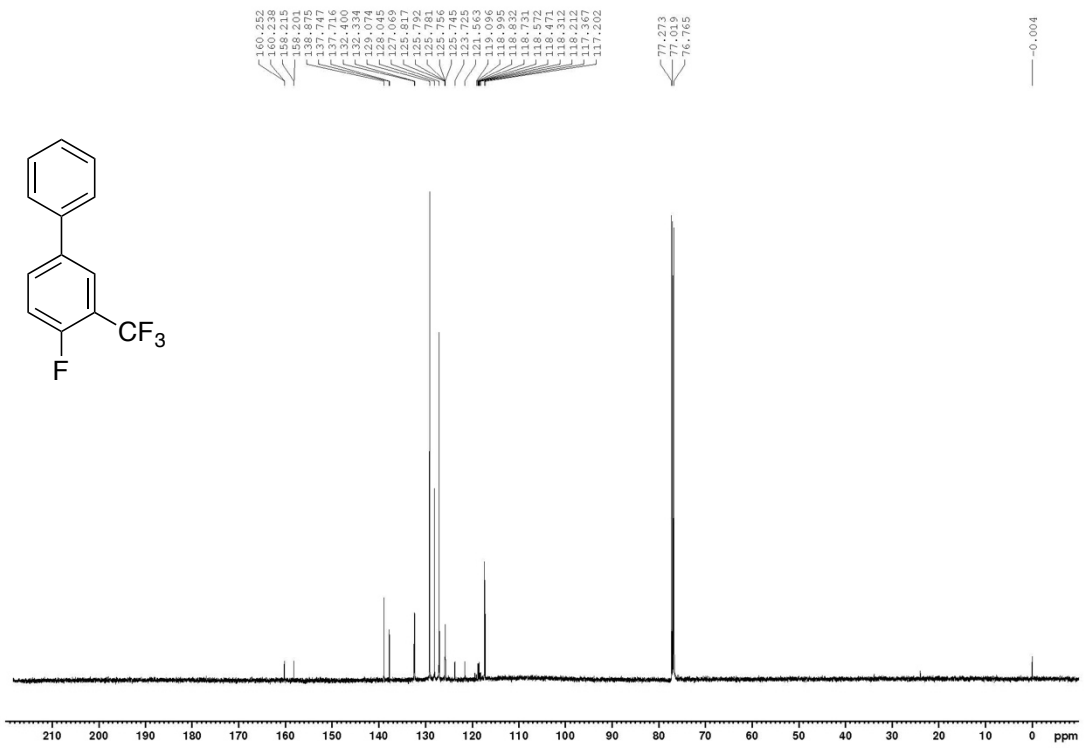

7.260
6.378
6.375
6.372
6.369
6.363
6.360
6.358
6.354
6.248
6.234
6.220
6.206
3.022
3.019
3.016
3.014
3.013
3.012
3.009
3.006
3.003
3.000
2.999
2.998
2.997
2.995
2.992
2.989
1.536
0.068
-0.000
X
X
X = I
1.81
1.90
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


136.837
84.327
77.252
76.998
76.744
40.690
-0.003
X
X
X = I
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.674
7.651
7.648
7.644
7.638
7.636
7.634
7.632
7.628
7.471
7.470
7.466
7.457
7.455
7.453
7.442
7.439
7.373
7.370
7.368
7.359
7.356
7.352
7.343
7.341
7.338
7.236
0.000
4.00
4.00
4.09
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


140.696
140.114
128.807
127.492
127.333
127.043
77.259
77.005
76.750
0.005
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.788
7.785
7.783
7.744
7.743
7.739
7.738
7.735
7.733
7.730
7.728
7.727
7.726
7.722
7.721
7.717
7.716
7.713
7.711
7.547
7.546
7.543
7.539
7.532
7.531
7.529
7.527
7.526
7.522
7.479
7.478
7.476
7.472
7.465
7.464
7.463
7.461
7.458
7.449
7.447
7.446
7.445
7.408
7.406
7.403
7.395
7.381
7.379
7.377
7.281
7.262
7.248
7.243
1.534
1.297
1.283
0.000
CF3
F
0.99
1.00
2.04
2.03
0.96
1.17
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm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160.238
158.215
158.001
138.875
137.747
137.716
132.400
132.334
129.074
129.045
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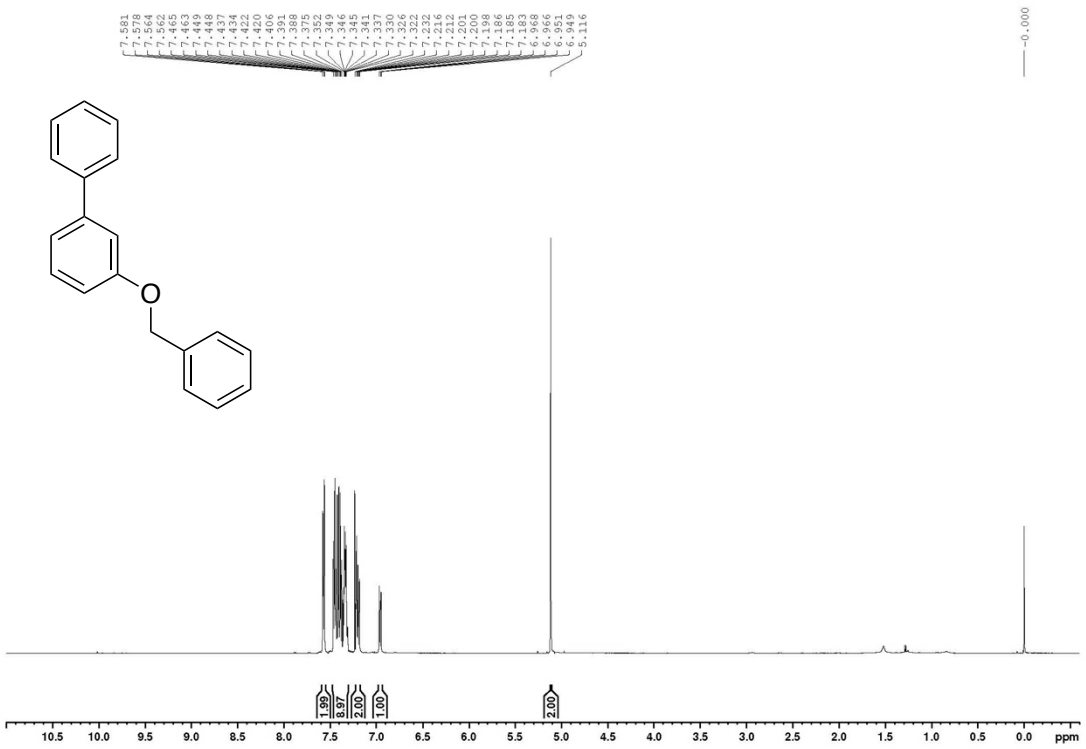
125.792
125.781
125.756
125.745
123.725
121.563
119.096
118.995
118.832
118.731
118.572
118.471
118.312
118.212
117.367
117.202
77.273
77.019
76.765
-0.004
CF3
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.581
7.578
7.564
7.562
7.465
7.463
7.449
7.448
7.437
7.434
7.422
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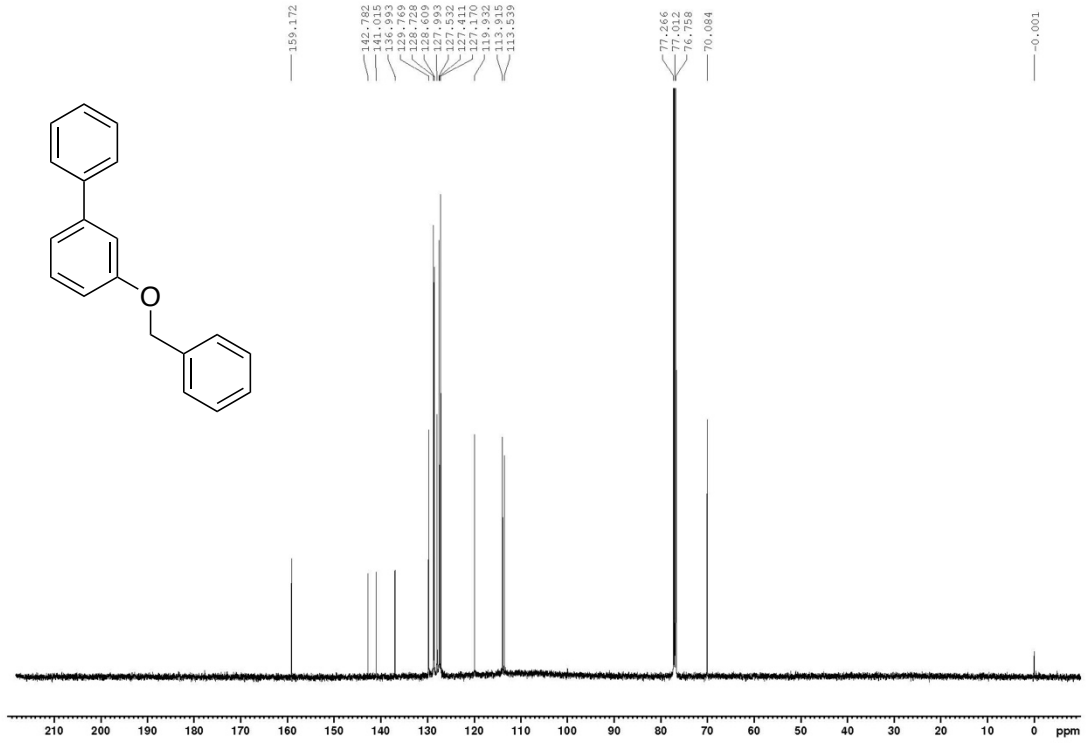
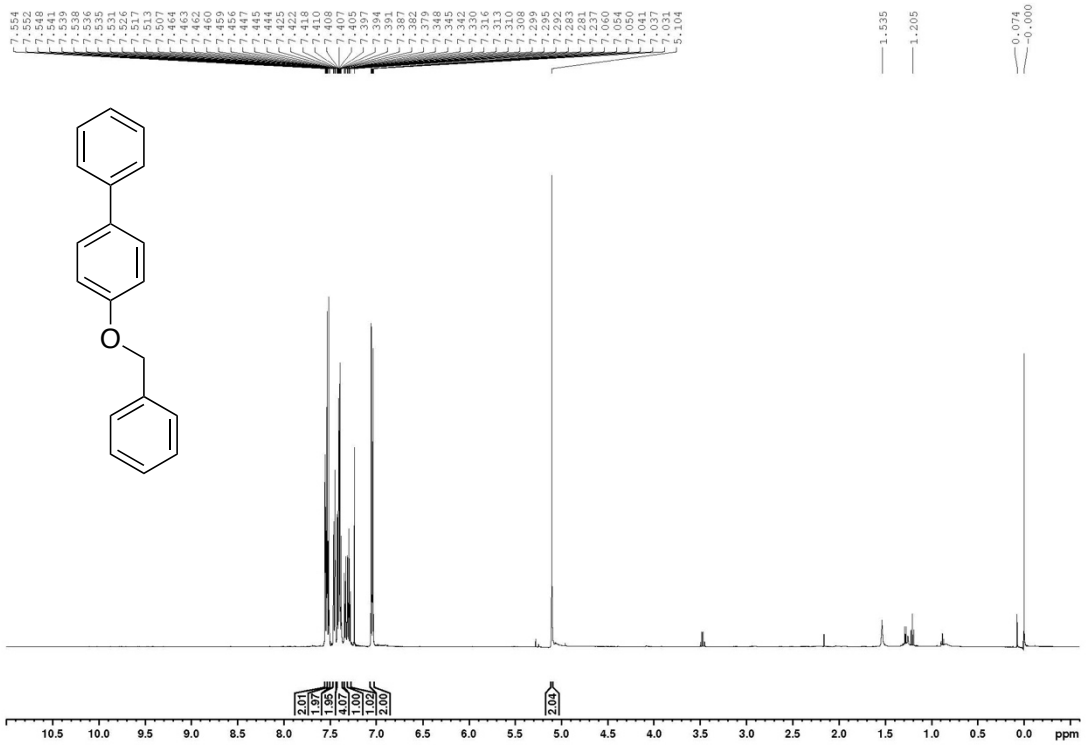
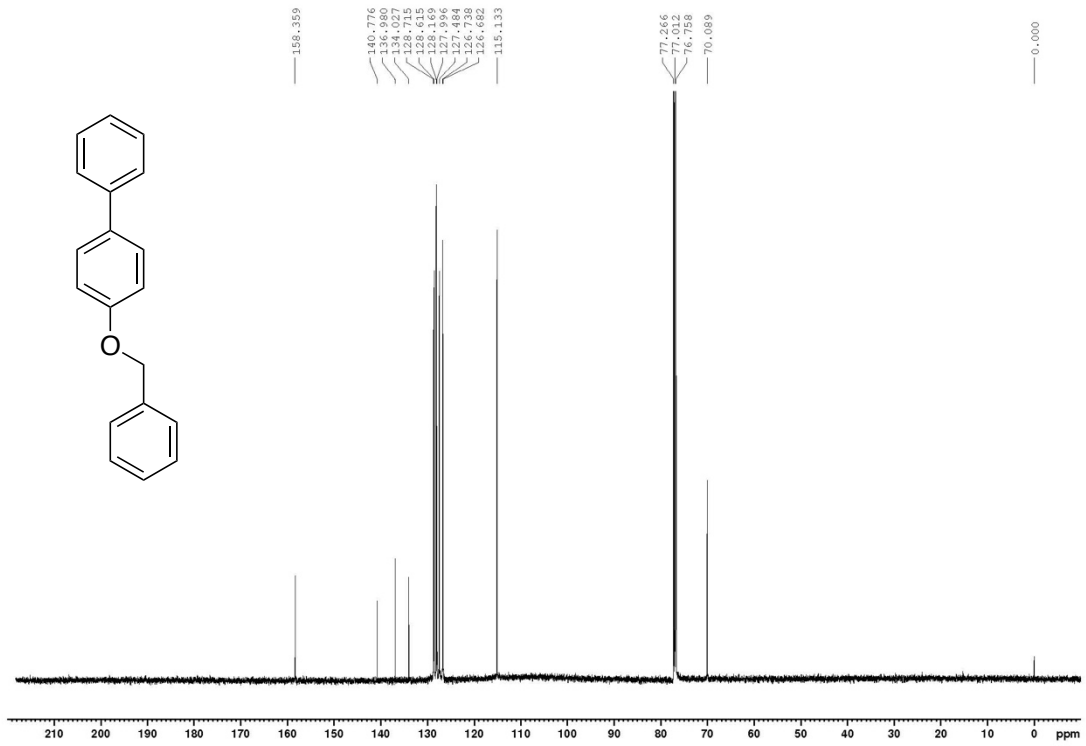
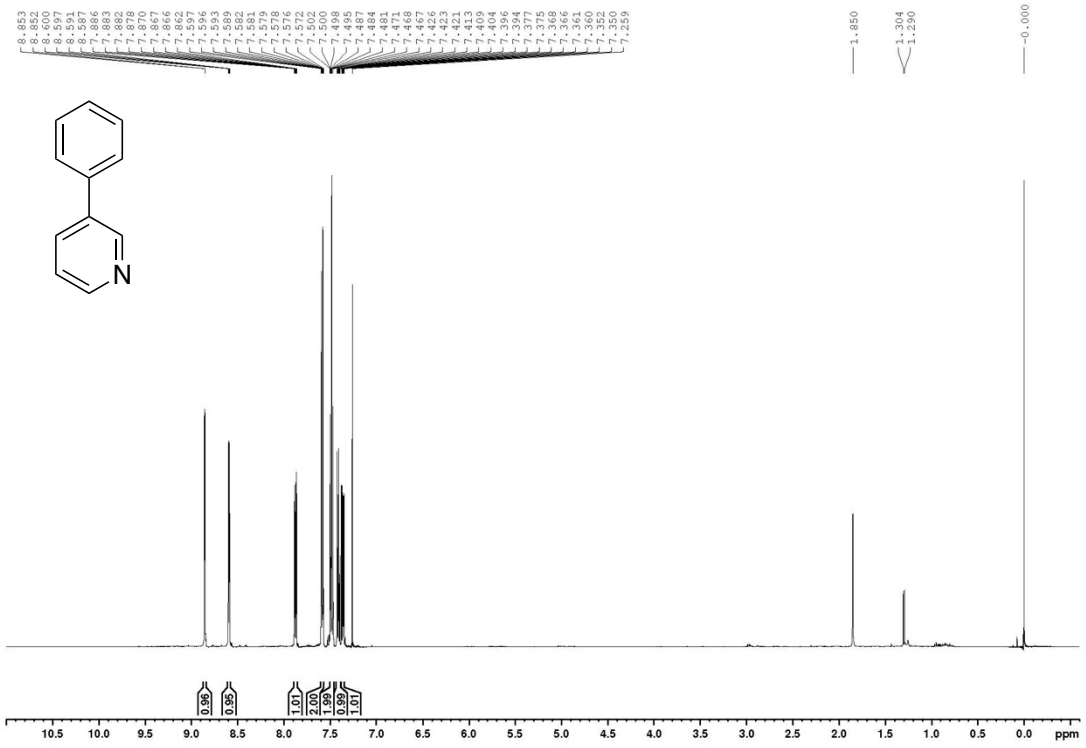
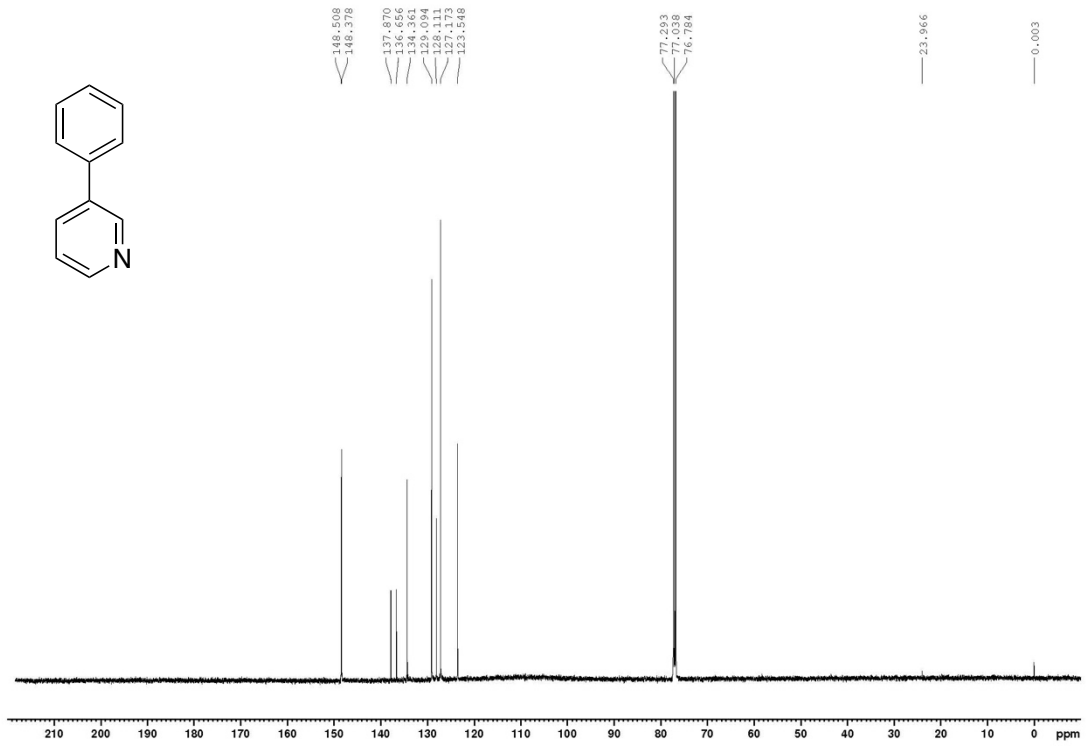
7.406
7.391
7.388
7.375
7.352
7.349
7.346
7.345
7.341
7.337
7.330
7.326
7.322
7.232
7.216
7.212
7.201
7.200
7.198
7.186
7.185
7.183
7.068
6.966
6.951
6.949
5.116
0.000
O
1.99
8.97
2.00
1.00
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

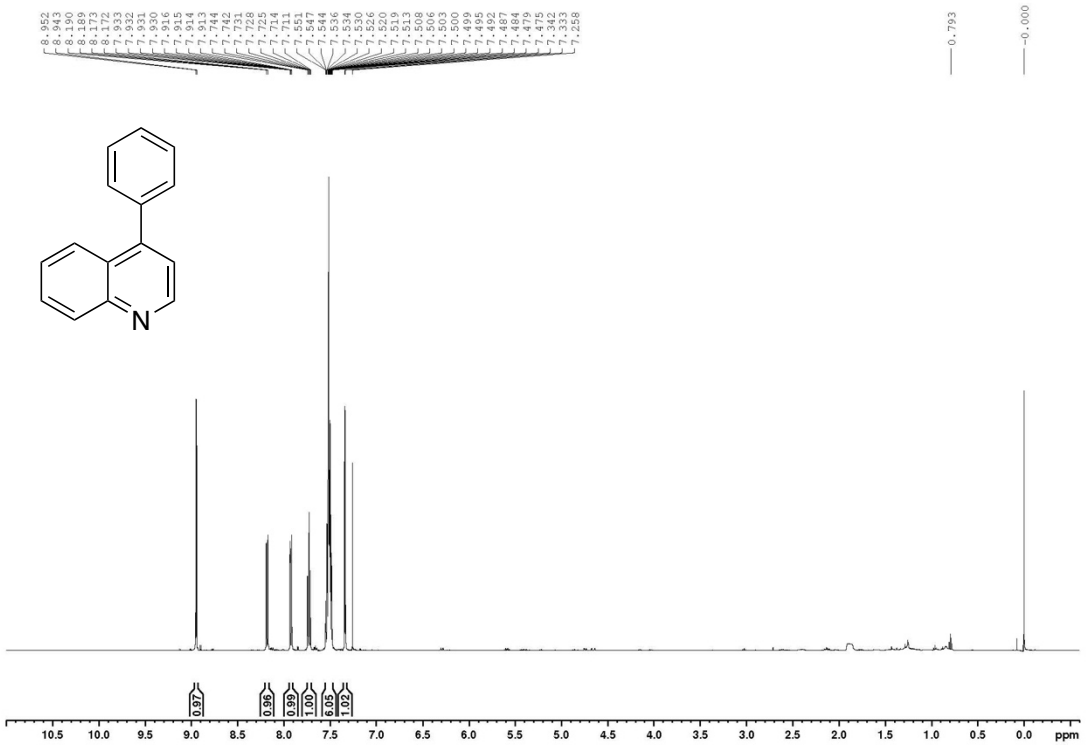

159.172
142.782
141.015
136.993
129.769
128.728
128.699
128.093
127.532
127.411
127.170
119.932
113.915
113.539
77.266
77.012
76.758
70.084
0.001
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

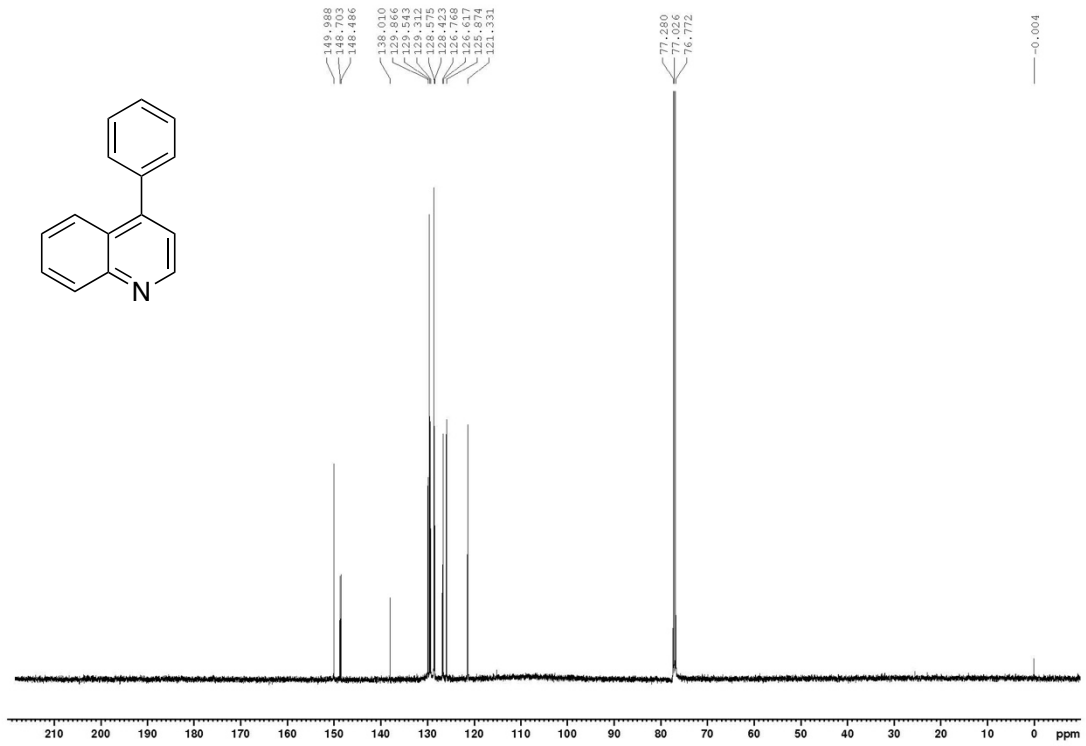

7.554
7.552
7.548
7.541
7.539
7.538
7.536
7.535
7.531
7.526
7.517
7.513
7.507
7.464
7.463
7.462
7.460
7.459
7.456
7.447
7.445
7.444
7.425
7.422
7.418
7.410
7.408
7.407
7.405
7.397
7.394
7.391
7.387
7.382
7.379
7.348
7.345
7.342
7.330
7.316
7.313
7.310
7.308
7.299
7.295
7.292
7.283
7.281
7.237
7.060
7.054
7.050
7.041
7.037
7.031
5.104
1.535
1.205
0.074
-0.000
O
2.01
1.97
1.95
4.07
1.00
1.02
2.00
2.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

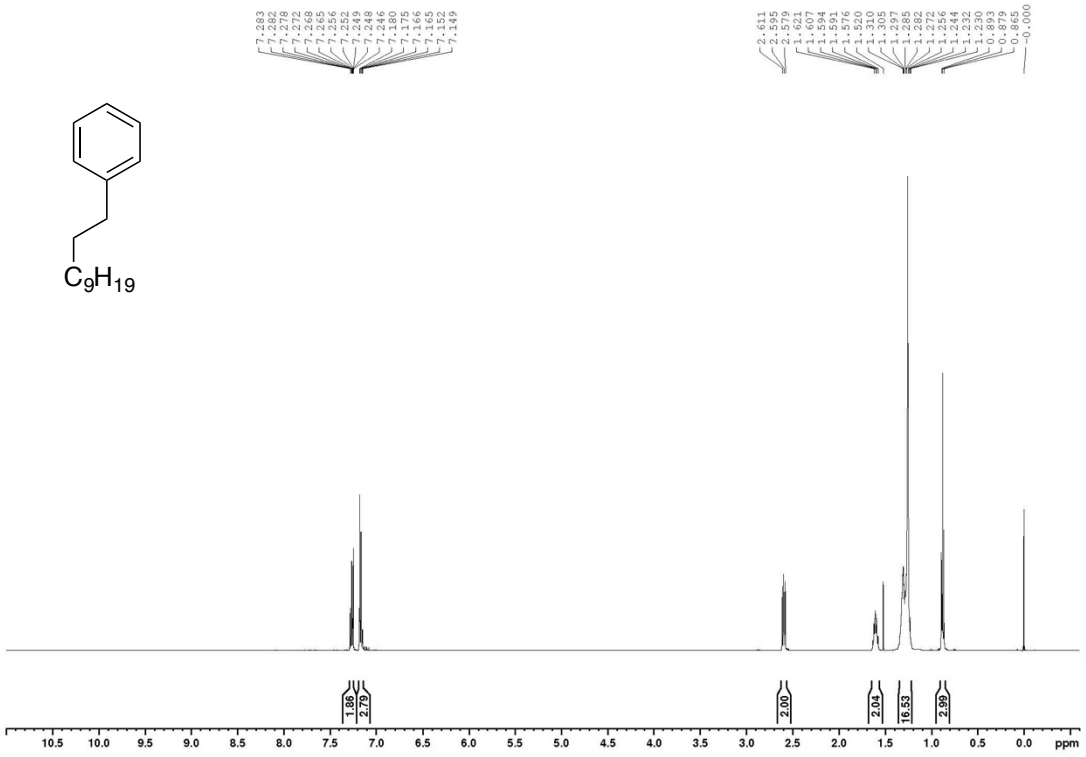

158.359
140.776
136.980
134.077
128.715
128.615
128.169
127.996
127.484
126.738
126.682
115.133
77.266
77.012
76.758
70.089
0.000
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

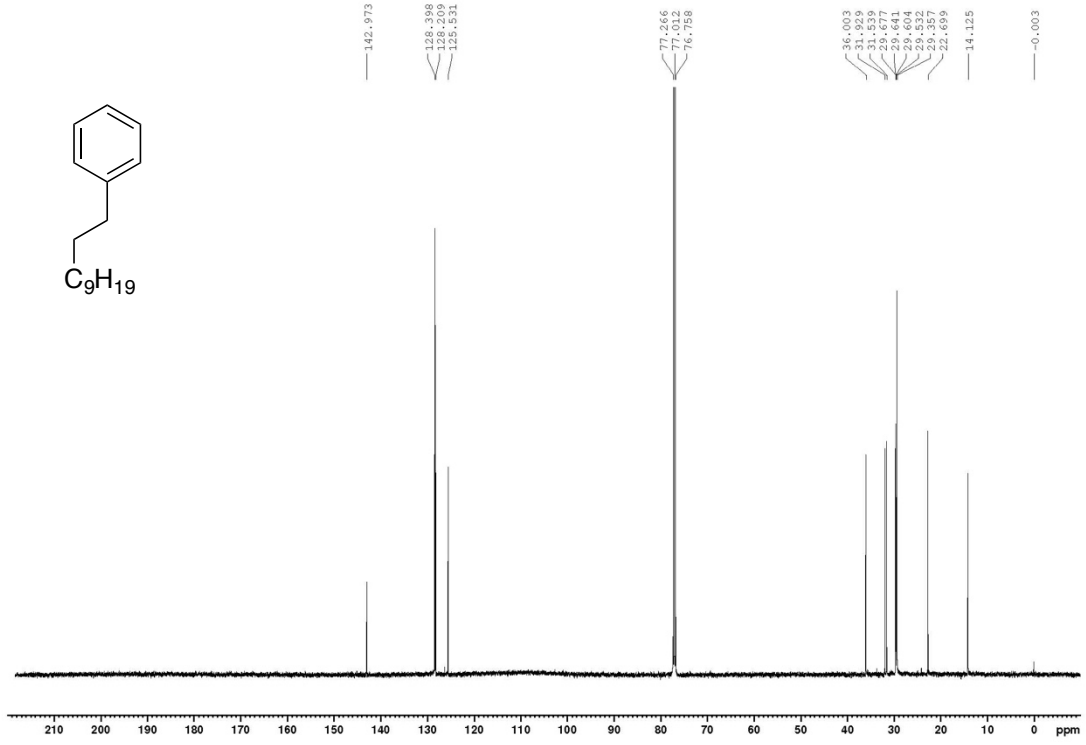

8.853
8.852
8.600
8.597
8.591
8.587
7.886
7.883
7.882
7.878
7.870
7.867
7.866
7.862
7.597
7.596
7.593
7.589
7.582
7.581
7.579
7.578
7.576
7.572
7.503
7.500
7.498
7.495
7.487
7.484
7.481
7.471
7.468
7.467
7.426
7.423
7.421
7.413
7.409
7.404
7.396
7.394
7.377
7.375
7.368
7.366
7.361
7.360
7.352
7.350
7.259
1.850
1.304
1.290
0.000
N
0.96
0.95
1.01
2.00
1.99
0.89
1.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

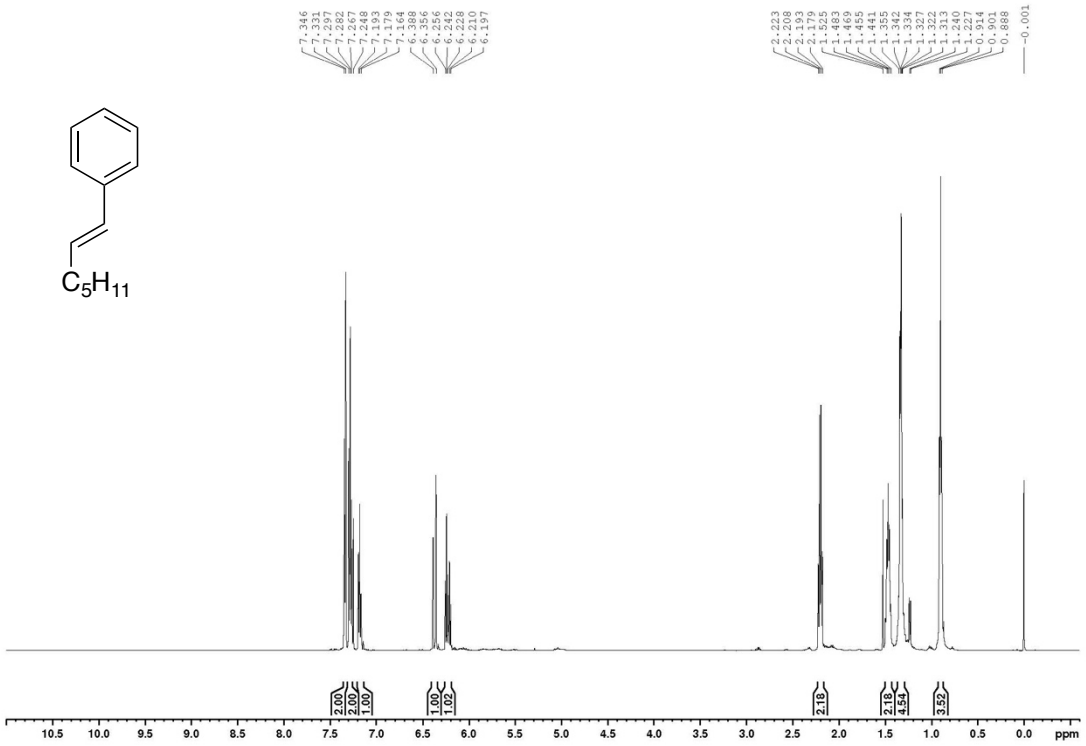

148.508
148.378
137.870
136.656
134.361
129.094
128.111
127.173
123.548
77.293
77.038
76.784
23.966
0.003
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

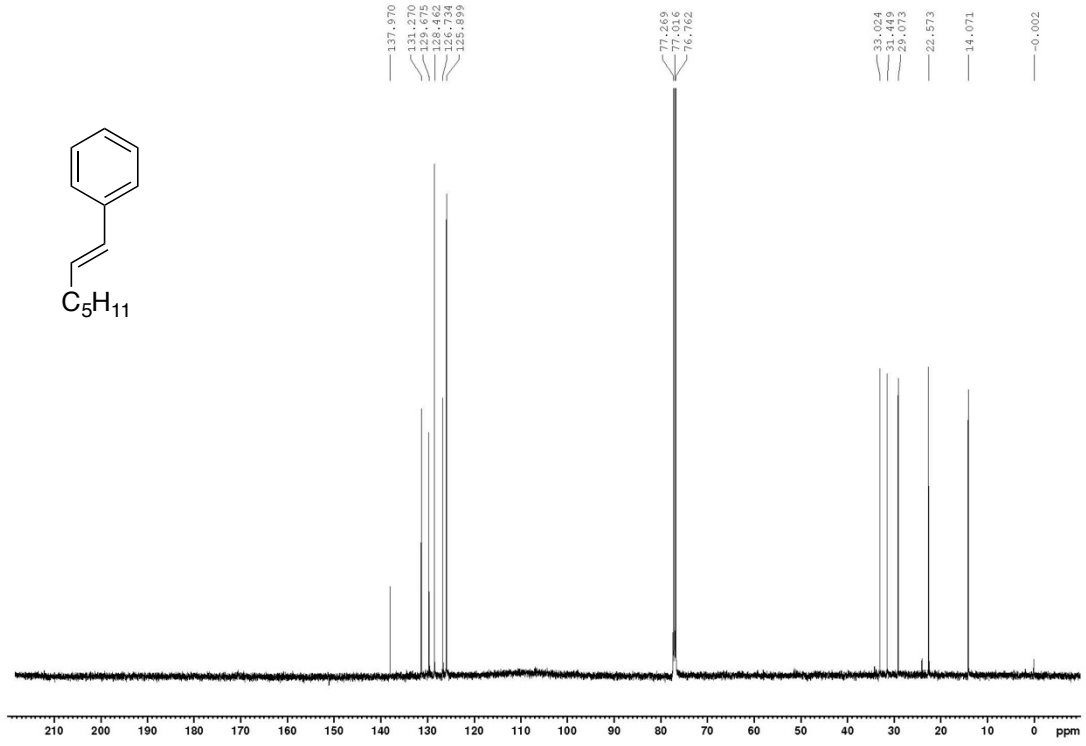

8.952
8.943
8.190
8.189
8.173
8.172
7.933
7.932
7.931
7.930
7.916
7.915
7.914
7.913
7.744
7.742
7.731
7.728
7.725
7.714
7.711
7.551
7.547
7.544
7.536
7.534
7.530
7.526
7.520
7.519
7.513
7.508
7.506
7.503
7.500
7.499
7.495
7.492
7.487
7.484
7.479
7.475
7.342
7.333
7.258
0.793
0.000
N
0.97
0.96
0.99
1.00
6.05
1.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

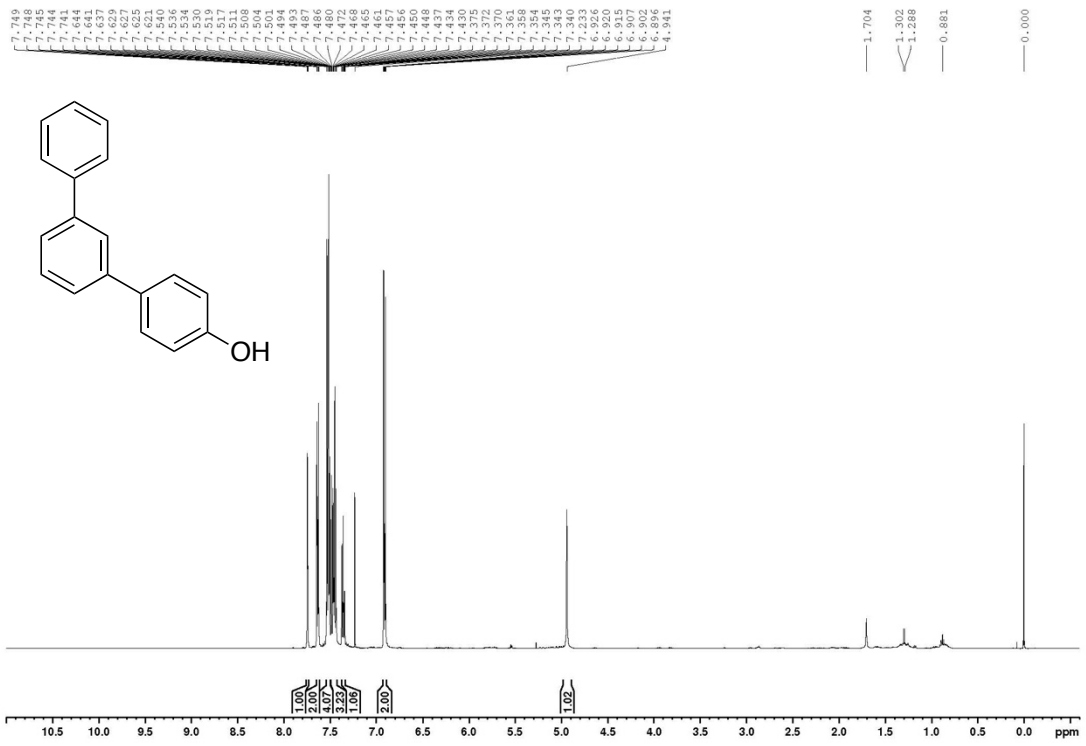

149.988
148.703
148.486
138.010
129.866
129.543
129.312
128.575
128.423
126.768
126.617
125.874
121.331
77.280
77.026
76.772
0.004
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

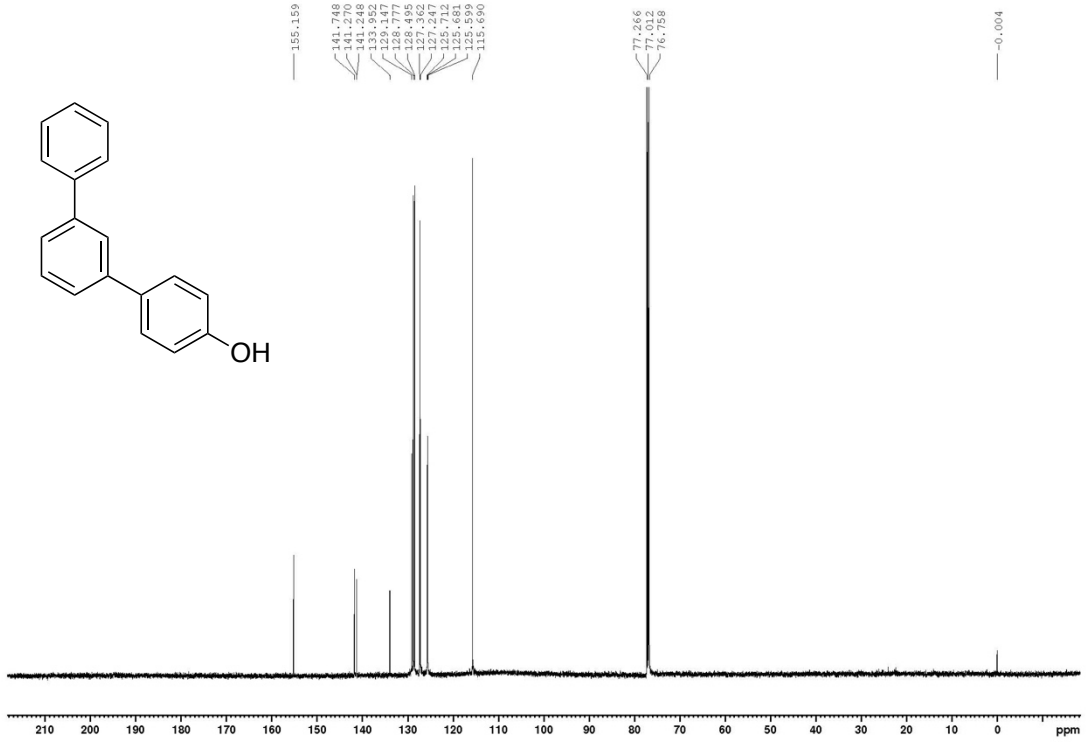

7.283
7.282
7.278
7.272
7.268
7.265
7.256
7.252
7.249
7.248
7.246
7.180
7.175
7.166
7.165
7.152
7.149
2.611
2.595
2.579
1.621
1.607
1.594
1.591
1.576
1.560
1.310
1.305
1.297
1.285
1.282
1.272
1.256
1.244
1.232
1.230
0.893
0.879
0.865
-0.000
C_9H_{19}
1.86
2.79
2.00
2.04
16.53
2.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

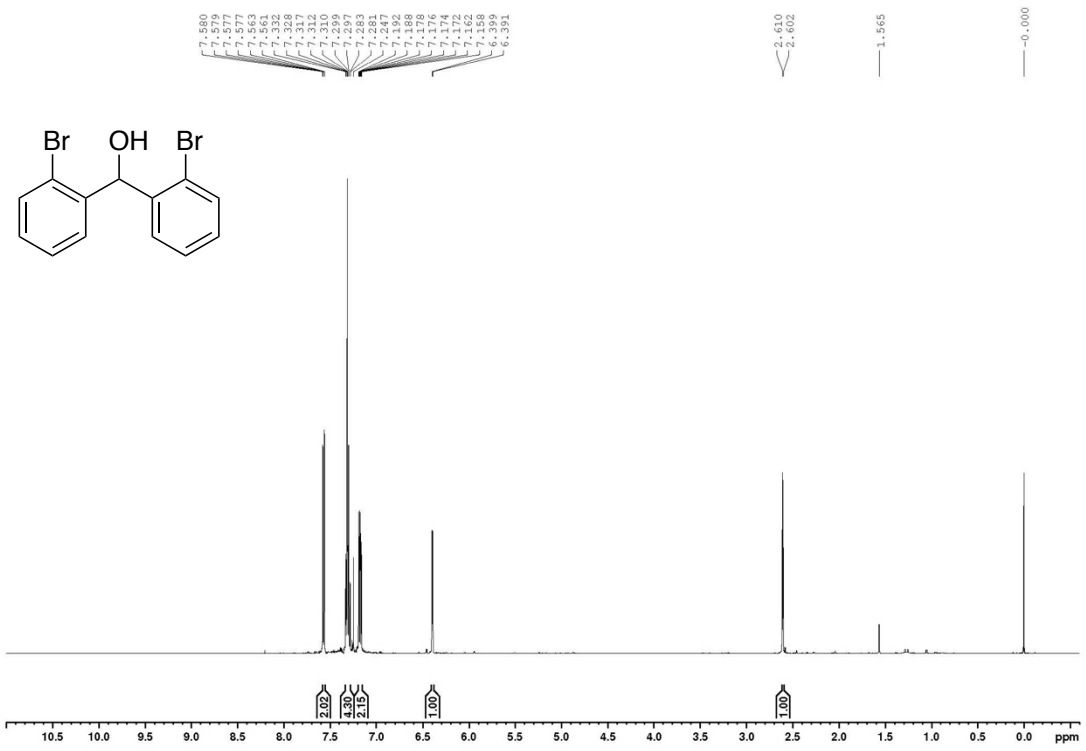

142.973
128.398
128.209
125.531
77.266
77.012
76.758
36.003
31.929
31.558
29.677
29.641
29.604
29.532
29.357
22.699
14.125
-0.003
C_9H_{19}
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

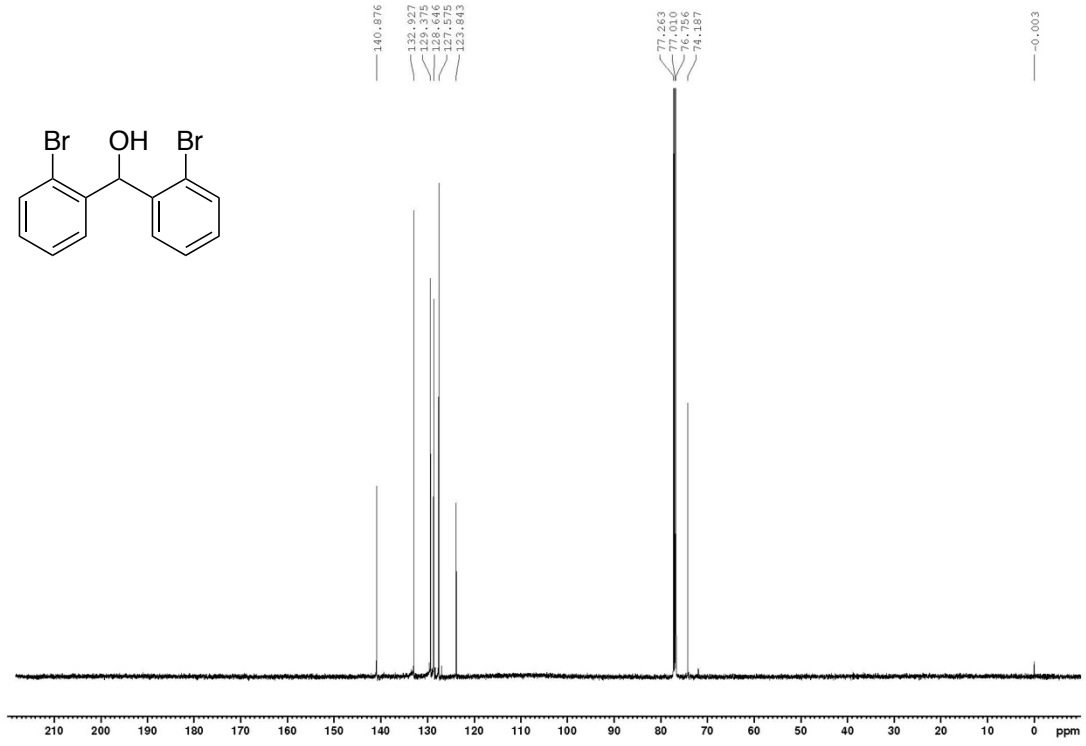

7.346
7.331
7.297
7.282
7.267
7.248
7.193
7.179
7.164
6.388
6.356
6.256
6.242
6.228
6.210
6.197
2.223
2.208
2.193
2.179
1.525
1.483
1.469
1.455
1.441
1.355
1.342
1.334
1.327
1.322
1.313
1.240
1.227
0.914
0.901
0.888
0.001
C_5H_{11}
2.00
2.00
1.00
1.00
1.02
2.18
2.18
4.54
3.52
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

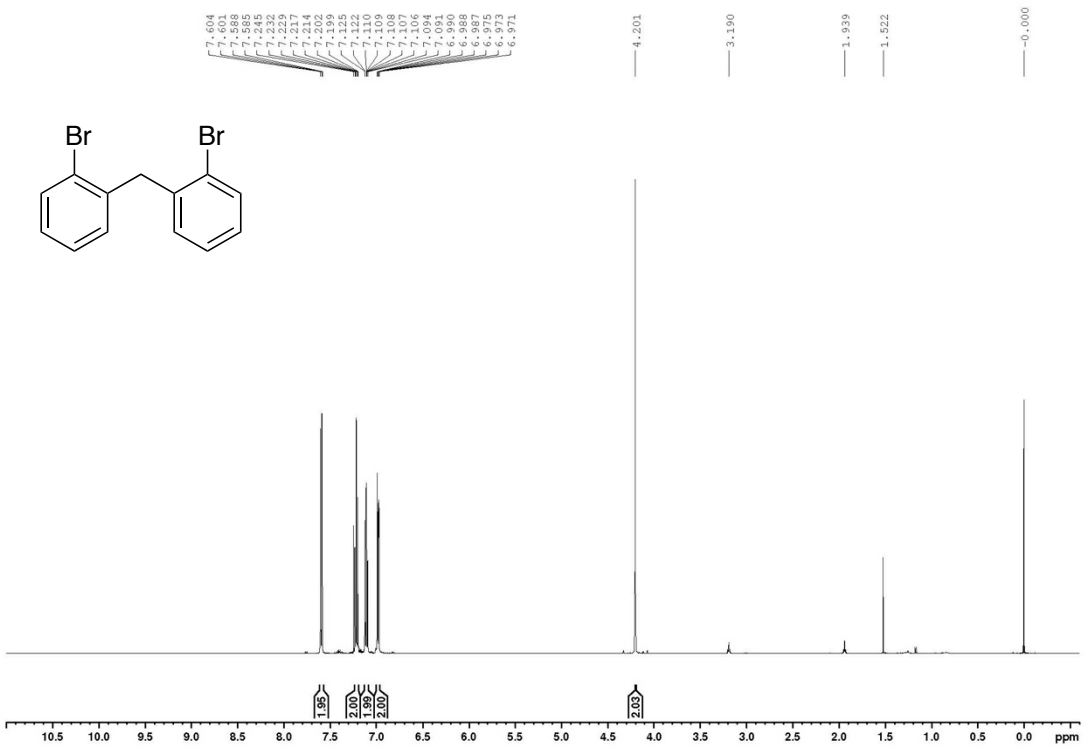

137.970
131.270
129.475
128.462
126.734
125.899
77.269
77.016
76.762
33.024
31.449
29.073
22.573
14.071
0.002
C_5H_{11}
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

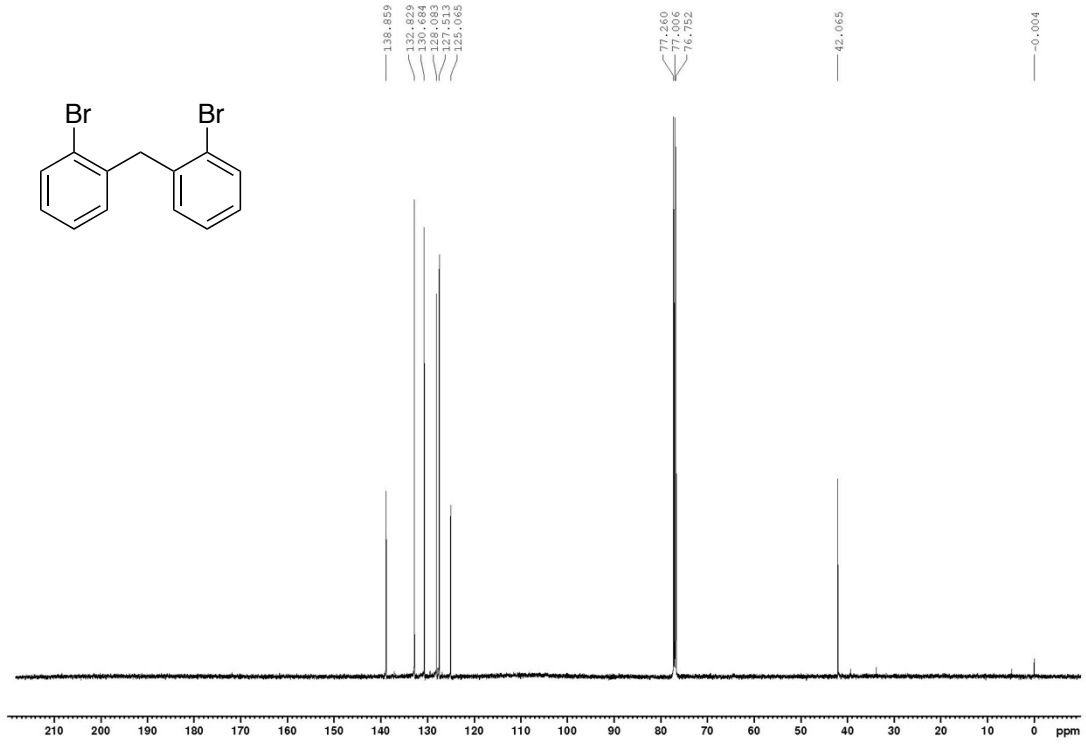

OH
ppm

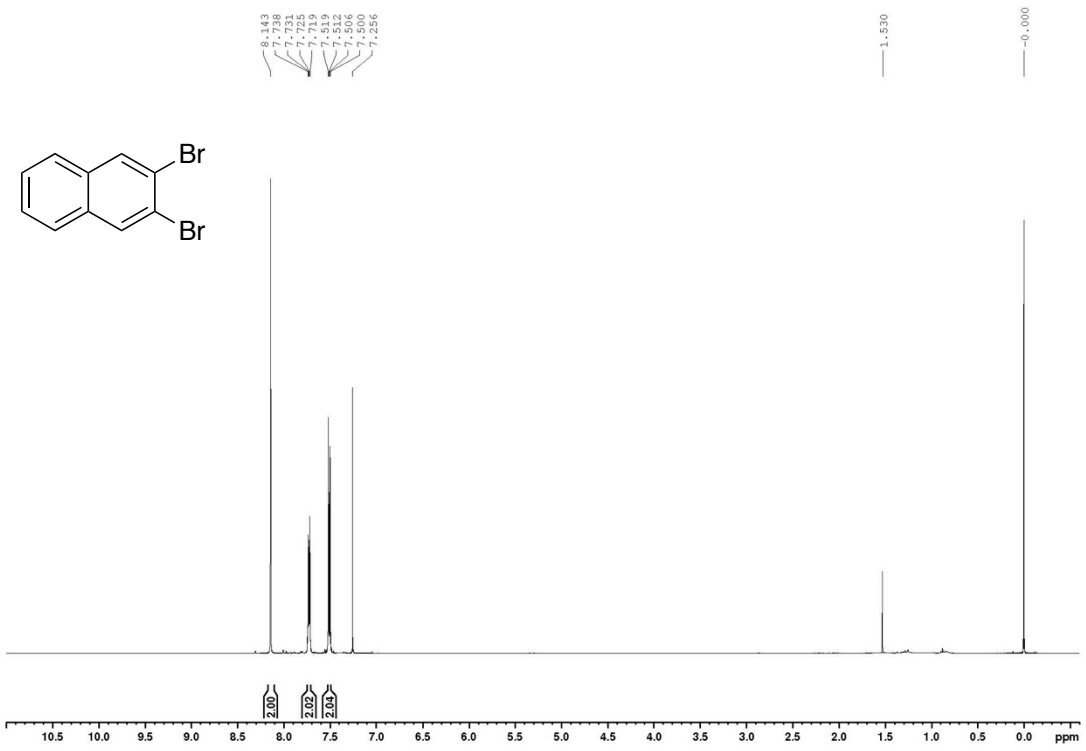

OH
ppm

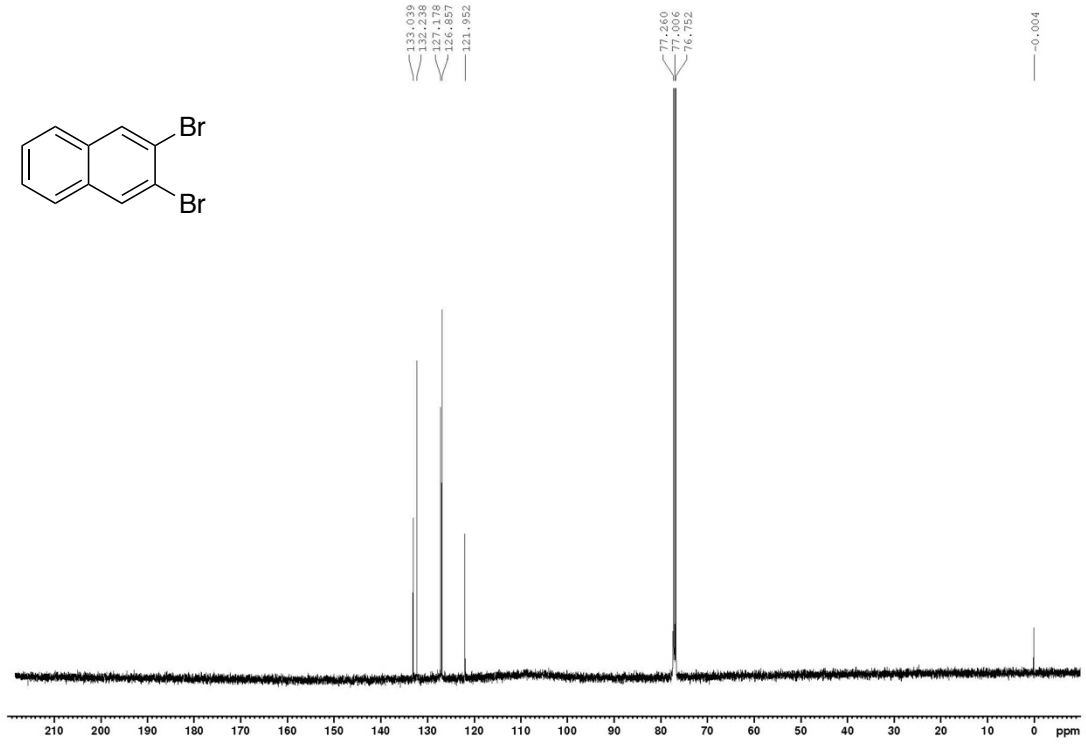

7.580
7.579
7.577
7.577
7.563
7.561
7.332
7.328
7.317
7.312
7.310
7.299
7.297
7.283
7.281
7.247
7.192
7.188
7.178
7.176
7.174
7.172
7.162
7.158
7.399
6.391
2.610
2.602
1.565
0.000
Br
OH
Br
2.02
4.30
2.15
1.00
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

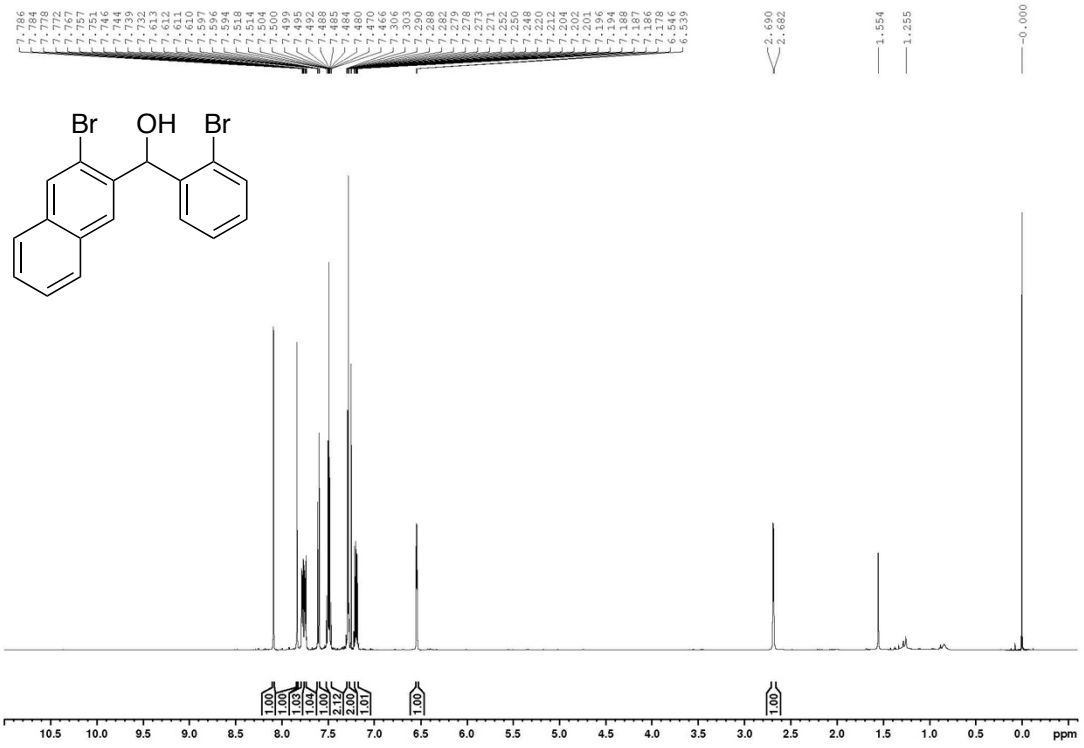

140.876
132.927
129.735
128.646
127.575
123.843
77.263
77.010
76.756
74.187
0.003
Br
OH
Br
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

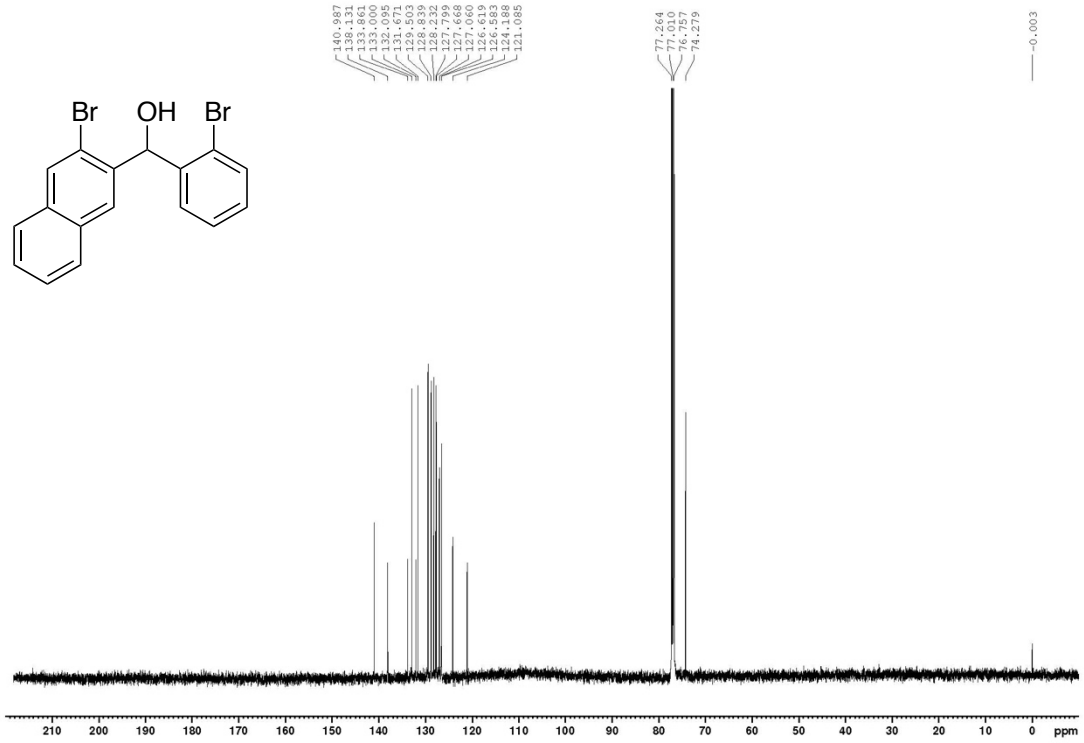

7.604
7.601
7.588
7.585
7.245
7.232
7.229
7.217
7.214
7.202
7.199
7.125
7.122
7.110
7.109
7.108
7.107
7.106
7.094
7.091
7.090
6.988
6.987
6.975
6.973
6.971
4.201
3.190
1.939
1.522
0.000
Br
Br
1.95
2.00
1.99
2.00
2.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

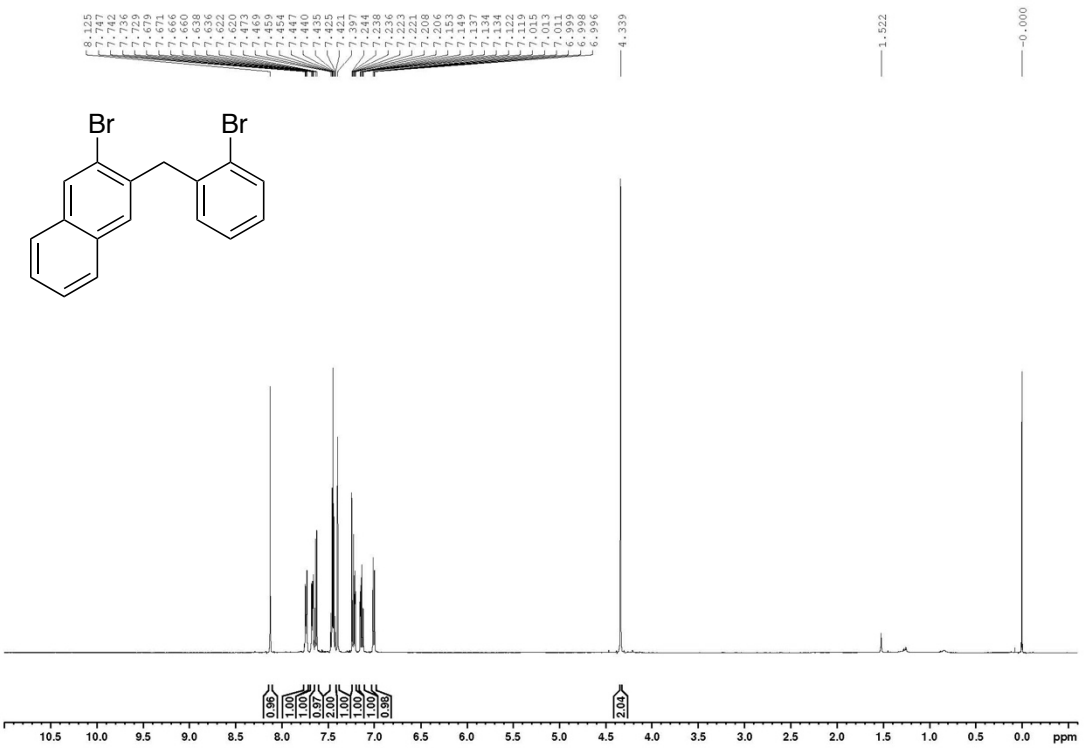

138.859
132.829
130.684
128.083
127.513
125.065
77.260
77.006
76.752
42.065
0.004
Br
Br
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

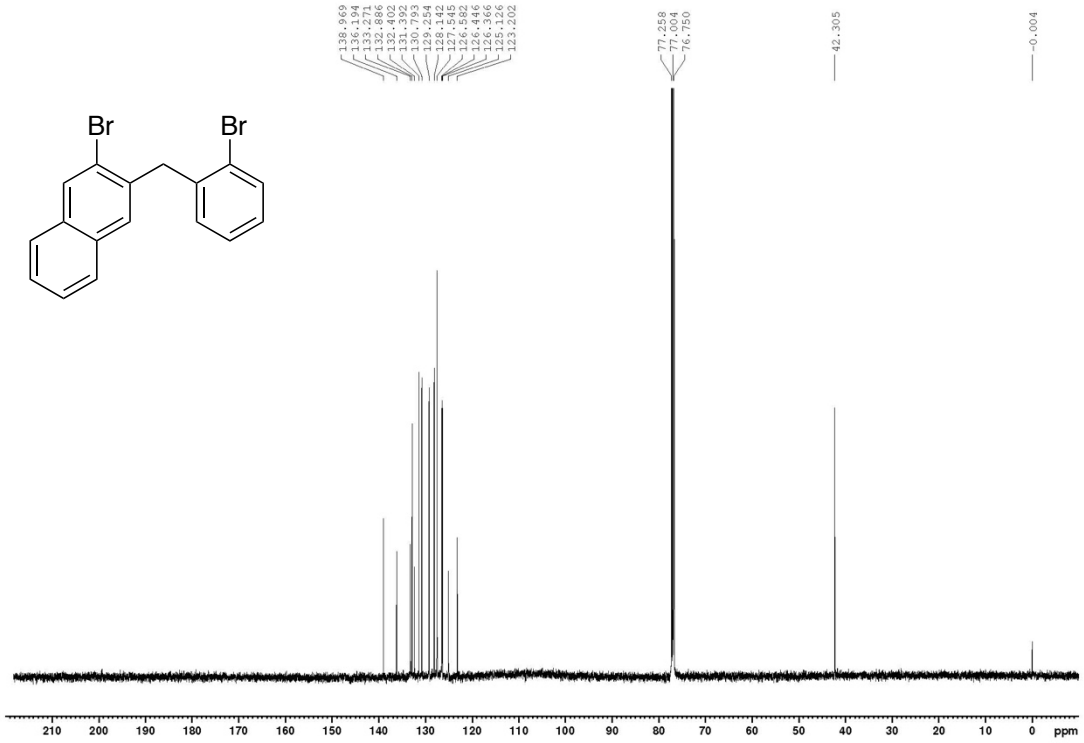

8.143
7.738
7.731
7.725
7.719
7.519
7.512
7.506
7.500
7.256
1.530
0.000
Br
Br
2.00
2.02
2.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


133.039
132.238
127.178
126.857
121.952
77.260
77.006
76.752
0.004
Br
Br
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

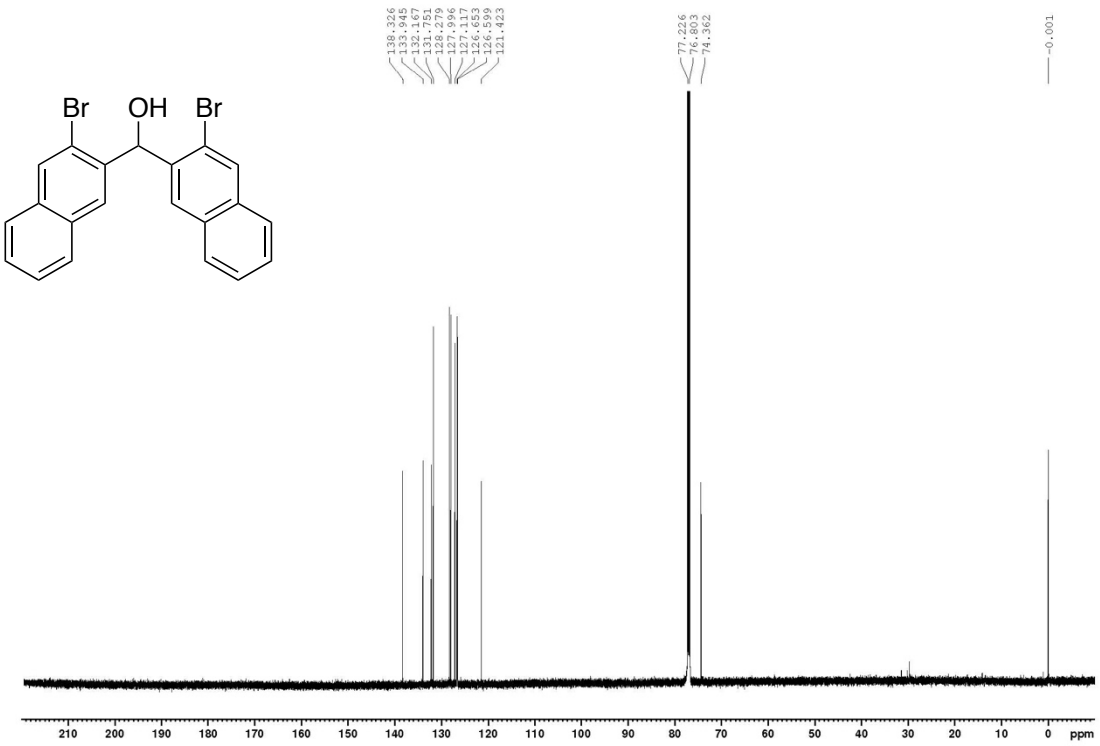

Br OH Br
7.786 7.784 7.778 7.772 7.767 7.757 7.751 7.746 7.744 7.739 7.733 7.613 7.612 7.611 7.610 7.597 7.596 7.594 7.518 7.514 7.504 7.500 7.499 7.495 7.488 7.485 7.484 7.480 7.470 7.466 7.306 7.303 7.290 7.288 7.282 7.279 7.278 7.273 7.271 7.252 7.250 7.248 7.220 7.212 7.204 7.202 7.201 7.196 7.194 7.188 7.187 7.186 7.178 6.546 6.539
2.690 2.682
1.554 1.255
0.000
1.00 1.00 1.03 1.04 1.00 2.19 2.00 1.01 1.00 1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

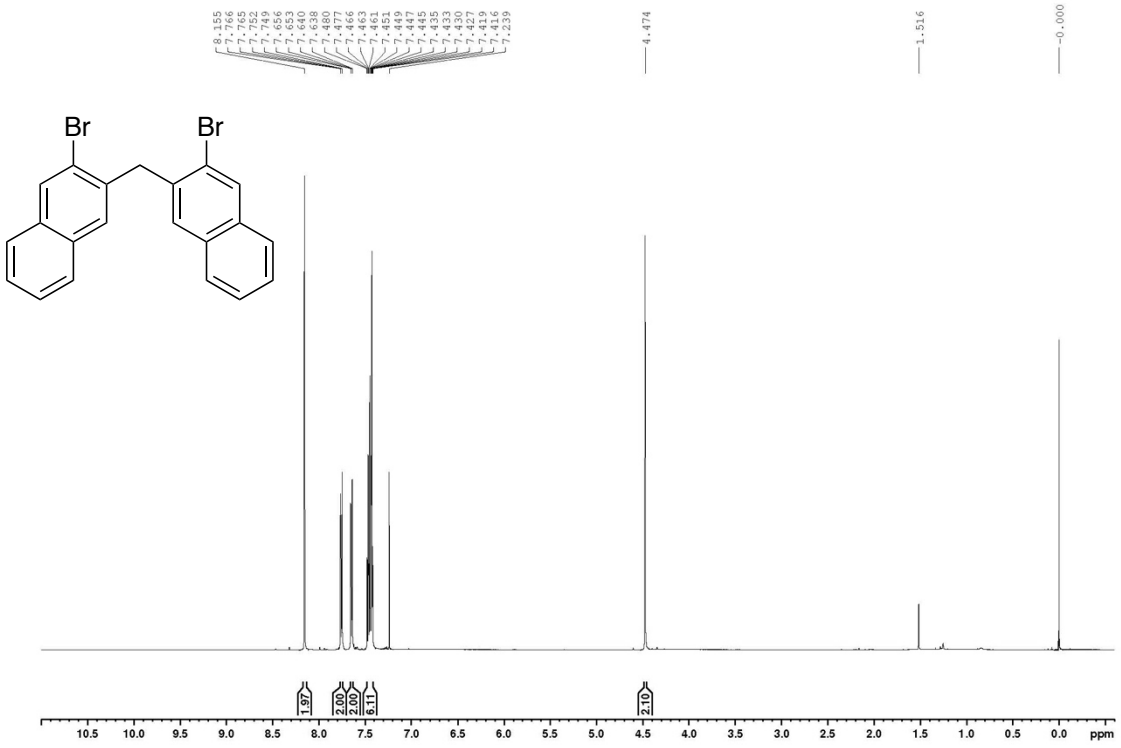

Br OH Br
140.987 138.131 133.861 133.000 132.095 131.671 129.503 128.839 128.232 127.799 127.668 127.060 126.619 126.583 124.188 121.085
77.264 77.010 76.757 74.279
0.003
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

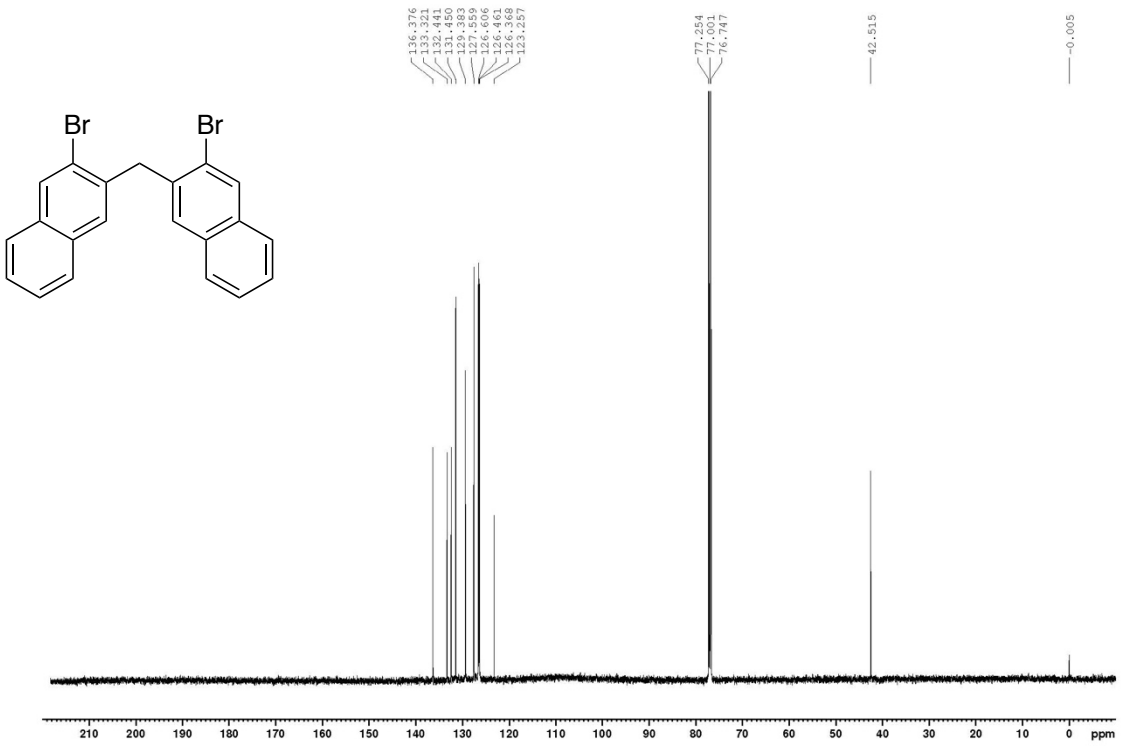

Br
Br
4.339
1.522
0.000
0.96
1.00
1.00
0.97
2.00
1.00
1.00
1.00
0.98
2.04
ppm


Br
Br
138.969
136.194
133.271
132.886
132.402
131.392
130.793
129.254
128.142
127.645
126.582
126.446
126.366
125.126
123.202
77.258
77.004
76.750
42.305
0.004
ppm


Br OH Br
8.134
7.810
7.787
7.785
7.768
7.749
7.747
7.534
7.531
7.520
7.517
7.515
7.505
7.503
7.492
7.488
7.486
7.483
7.472
7.470
7.458
7.456
6.691
2.739
2.730
1.537
1.253
0.070
-0.000
2.01
2.01
4.26
4.35
1.00
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


Br OH Br
138.326
133.945
132.167
131.751
128.279
127.996
127.117
126.653
126.599
121.423
77.226
76.803
74.362
-0.001
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.155
7.766
7.765
7.752
7.749
7.656
7.653
7.640
7.638
7.480
7.477
7.466
7.463
7.461
7.451
7.449
7.447
7.445
7.435
7.433
7.430
7.427
7.419
7.416
7.239
4.474
1.516
0.000
Br
Br
1.97
2.00
2.00
6.11
2.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm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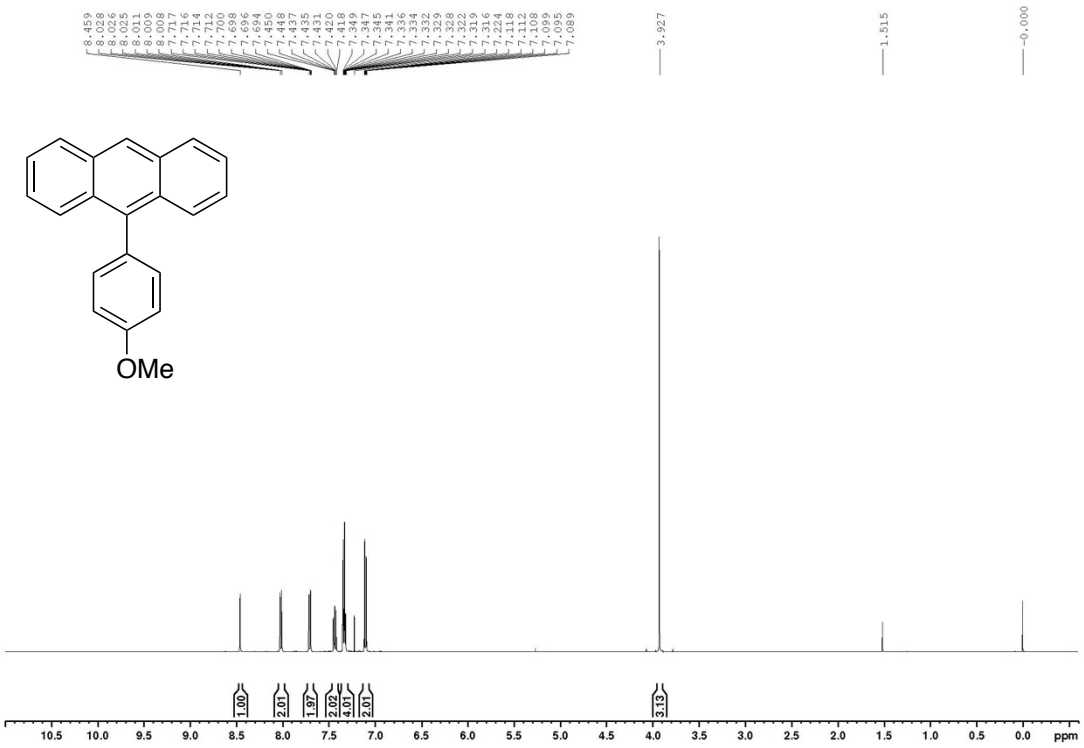
133.321
132.441
131.450
129.383
127.559
126.606
126.461
126.368
123.257
77.254
77.001
76.747
42.515
0.005
Br
Br
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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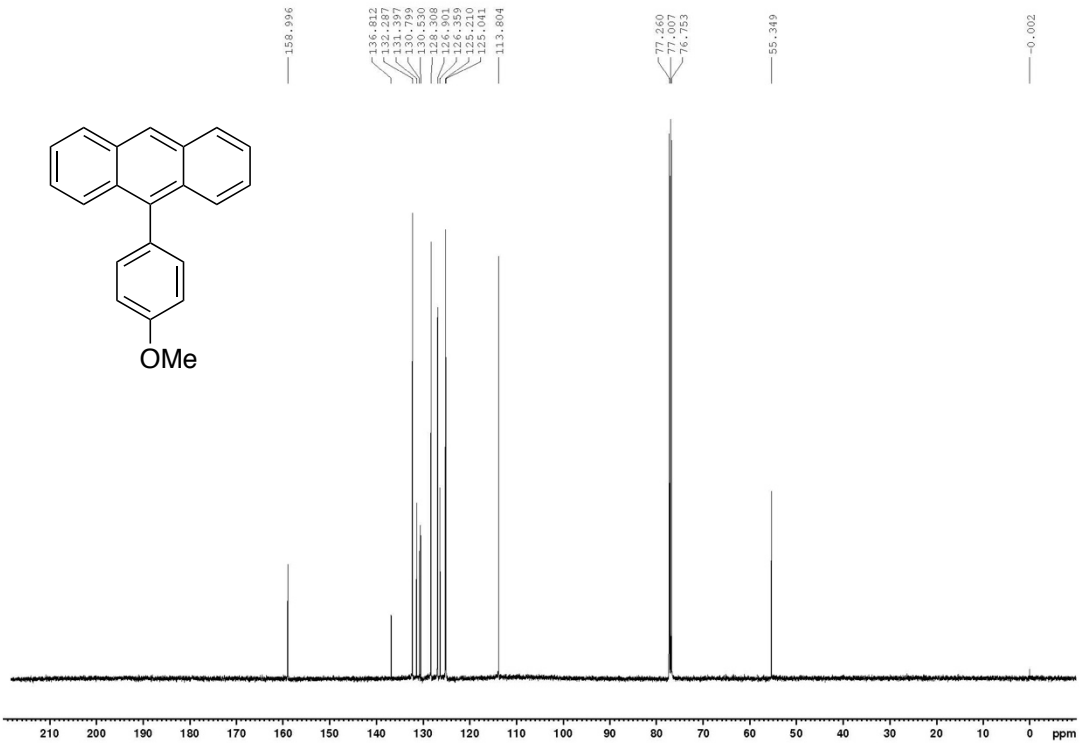
8.028
8.026
8.025
8.011
8.009
8.008
7.717
7.716
7.714
7.712
7.700
7.698
7.696
7.694
7.450
7.448
7.437
7.435
7.431
7.420
7.418
7.349
7.347
7.345
7.341
7.336
7.334
7.332
7.329
7.328
7.322
7.319
7.316
7.224
7.118
7.112
7.108
7.099
7.095
7.089
3.927
1.515
-0.000
OMe
1.00
2.01
1.97
2.02
4.01
2.01
3.13
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm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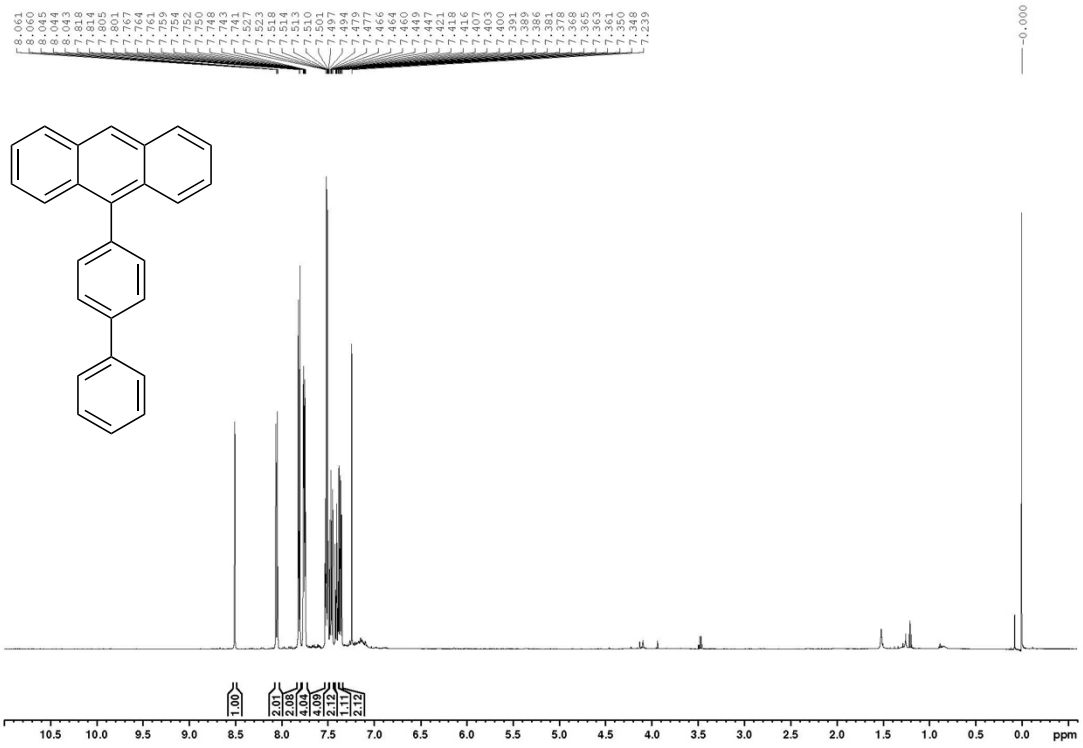
136.812
132.287
131.397
130.799
130.530
128.308
126.901
126.359
125.210
125.041
113.804
77.260
77.007
76.753
55.349
-0.002
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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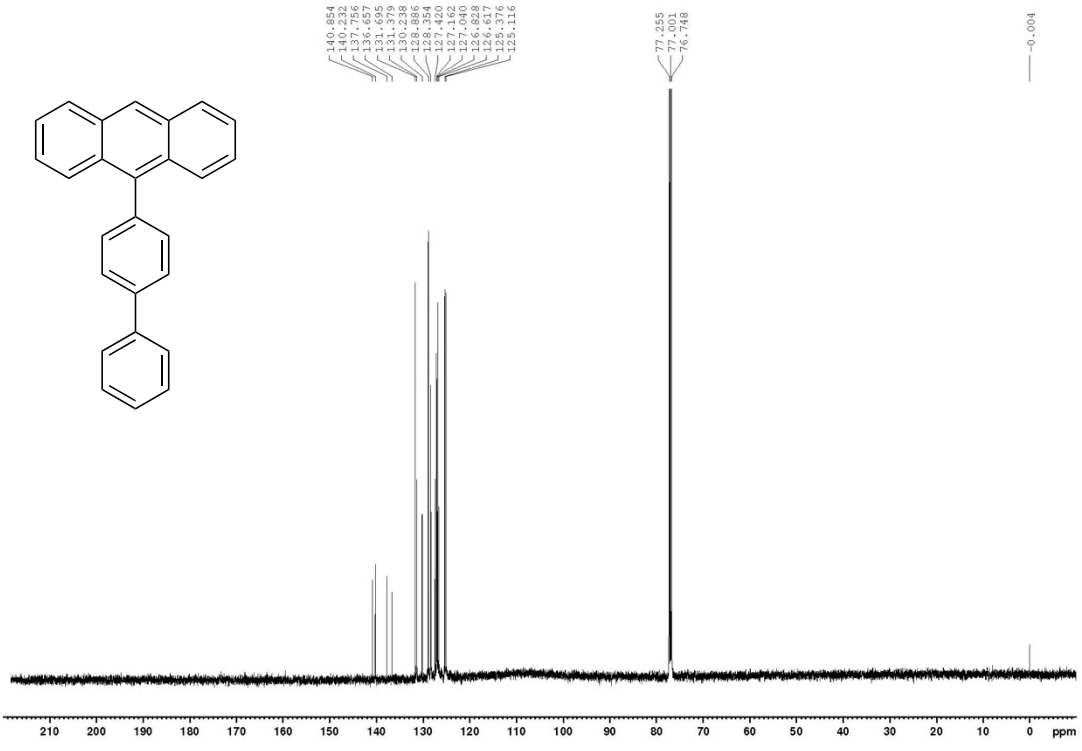
8.060
8.045
8.044
8.043
7.818
7.814
7.805
7.801
7.767
7.764
7.761
7.759
7.754
7.752
7.750
7.748
7.743
7.741
7.527
7.523
7.518
7.514
7.513
7.510
7.501
7.497
7.494
7.479
7.477
7.466
7.464
7.460
7.449
7.447
7.421
7.418
7.416
7.407
7.403
7.400
7.391
7.389
7.386
7.381
7.378
7.368
7.365
7.363
7.361
7.350
7.348
7.239
-0.000
1.00
2.01
2.08
4.04
4.09
2.12
1.11
2.12
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm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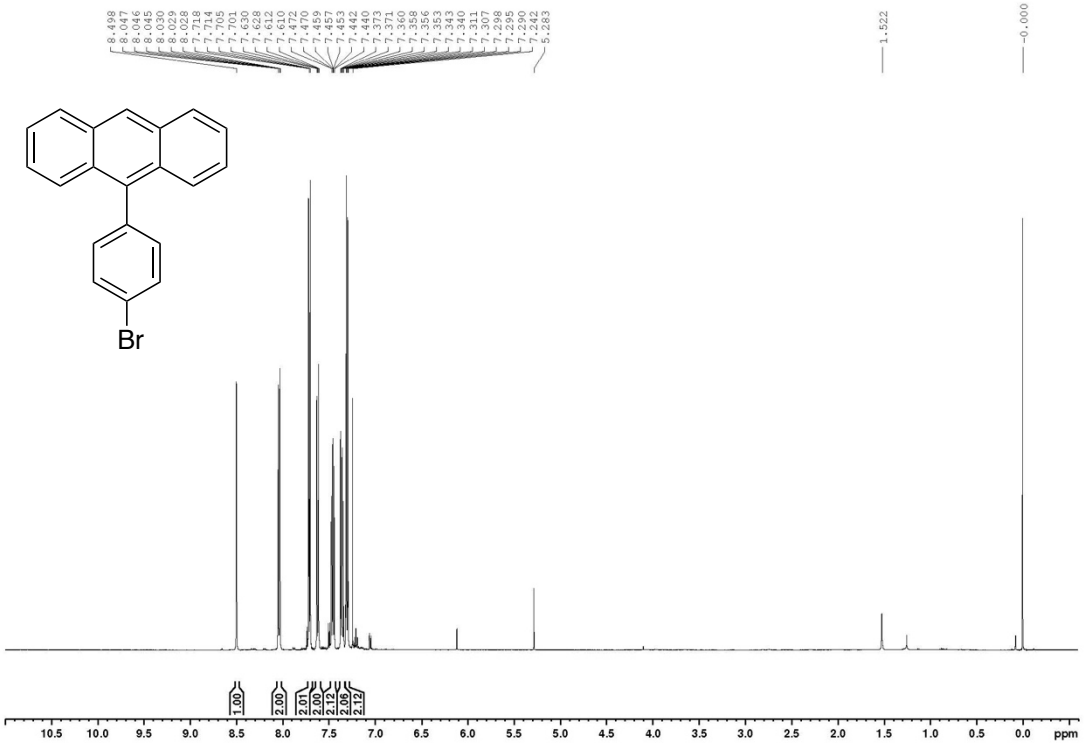
140.232
137.756
136.657
131.695
131.379
130.238
128.886
128.354
127.420
127.162
127.040
126.828
126.617
125.376
125.116
77.255
77.001
76.748
-0.004
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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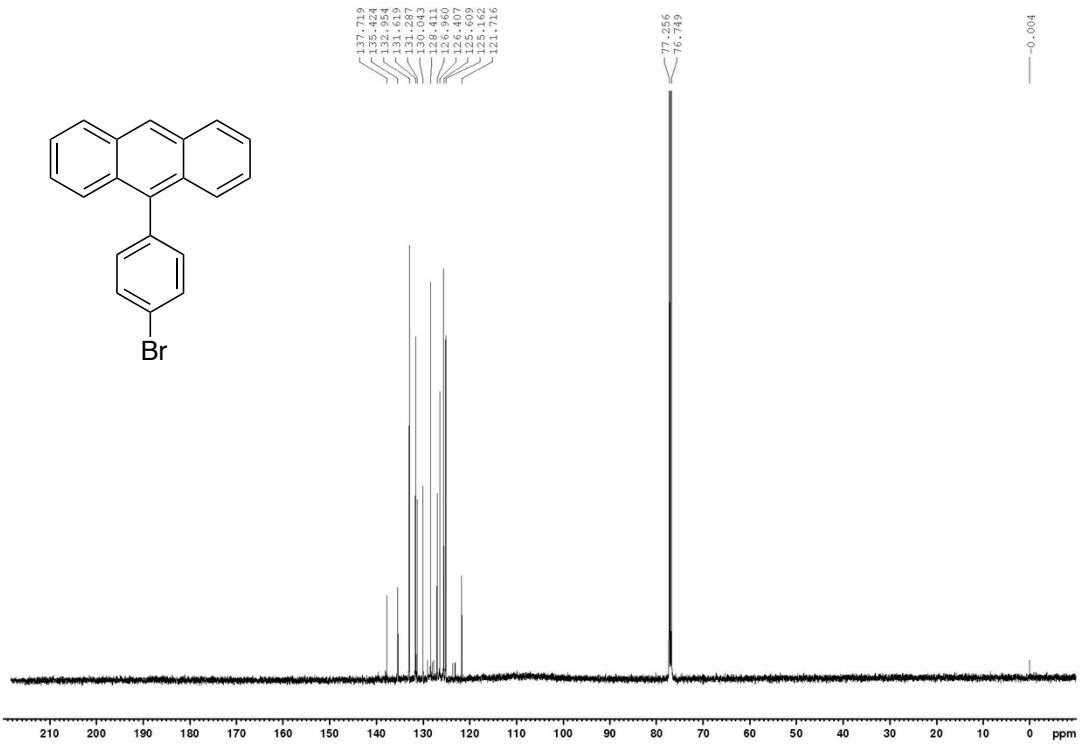
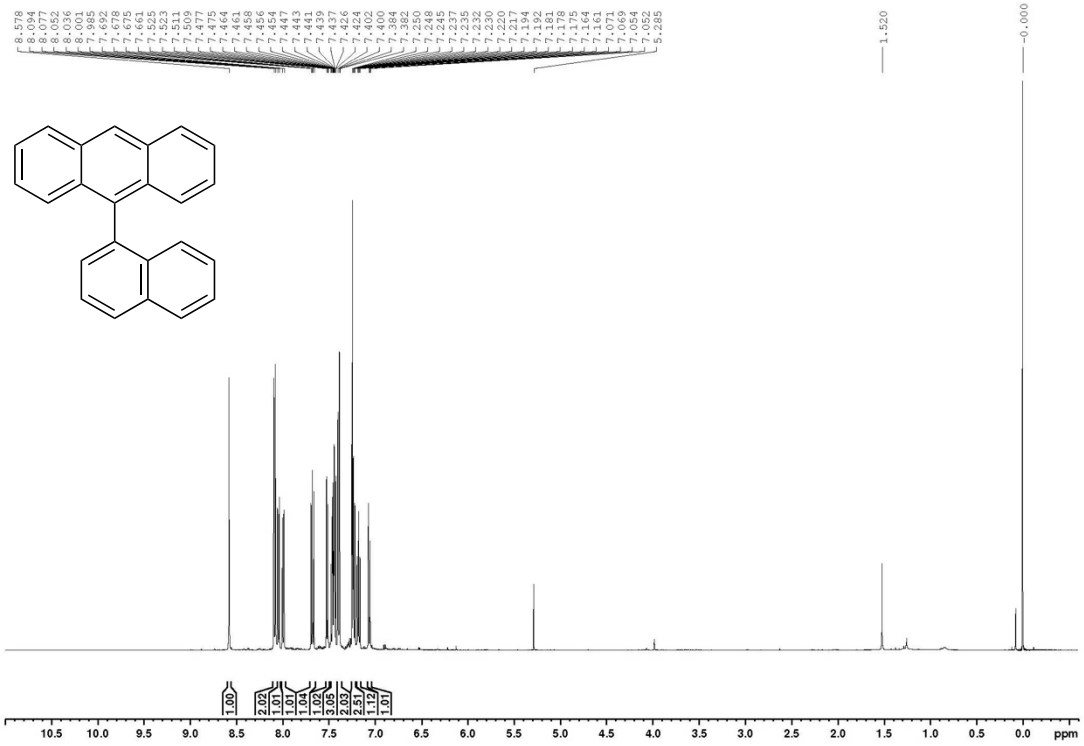
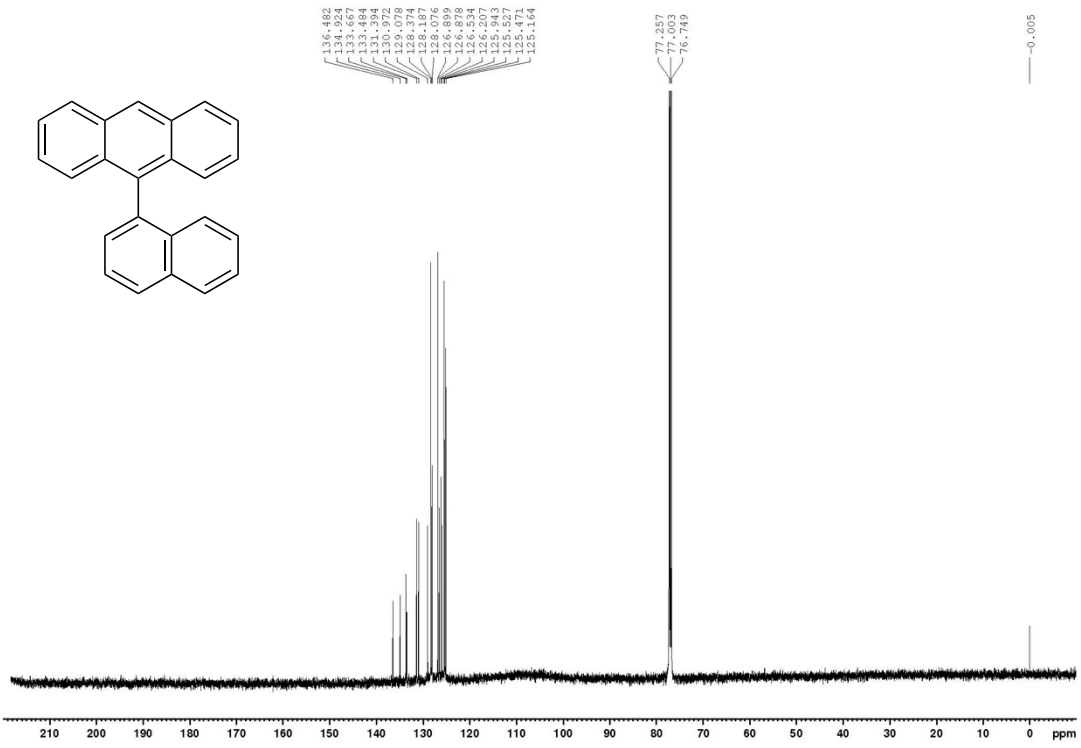
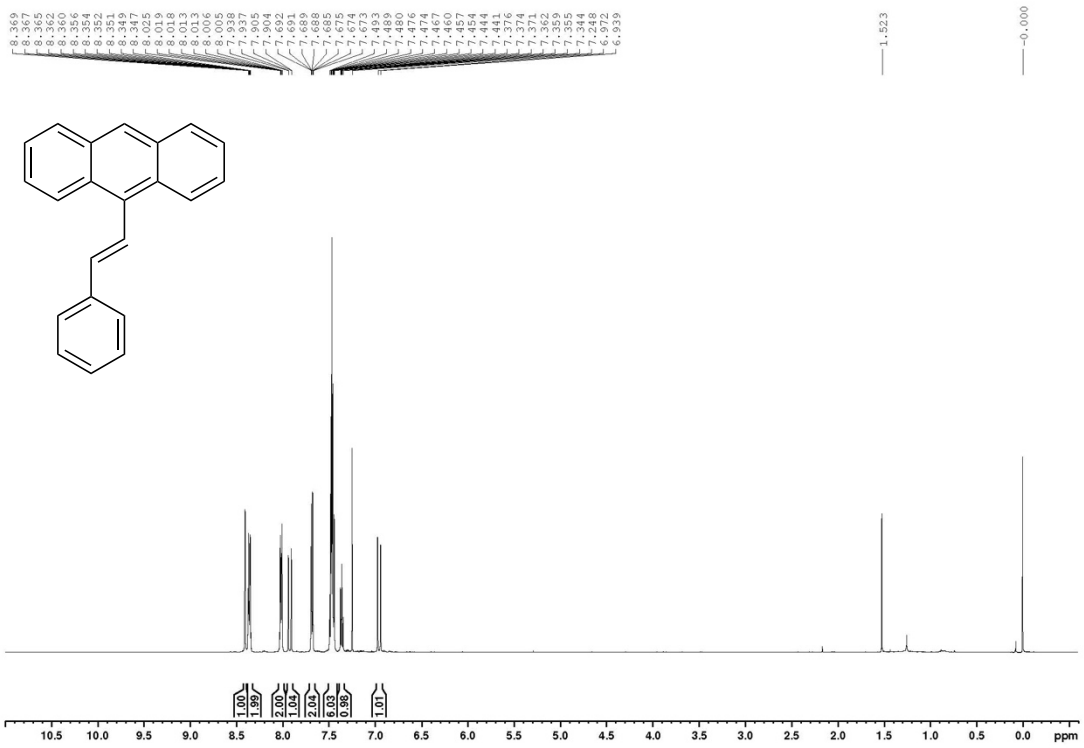
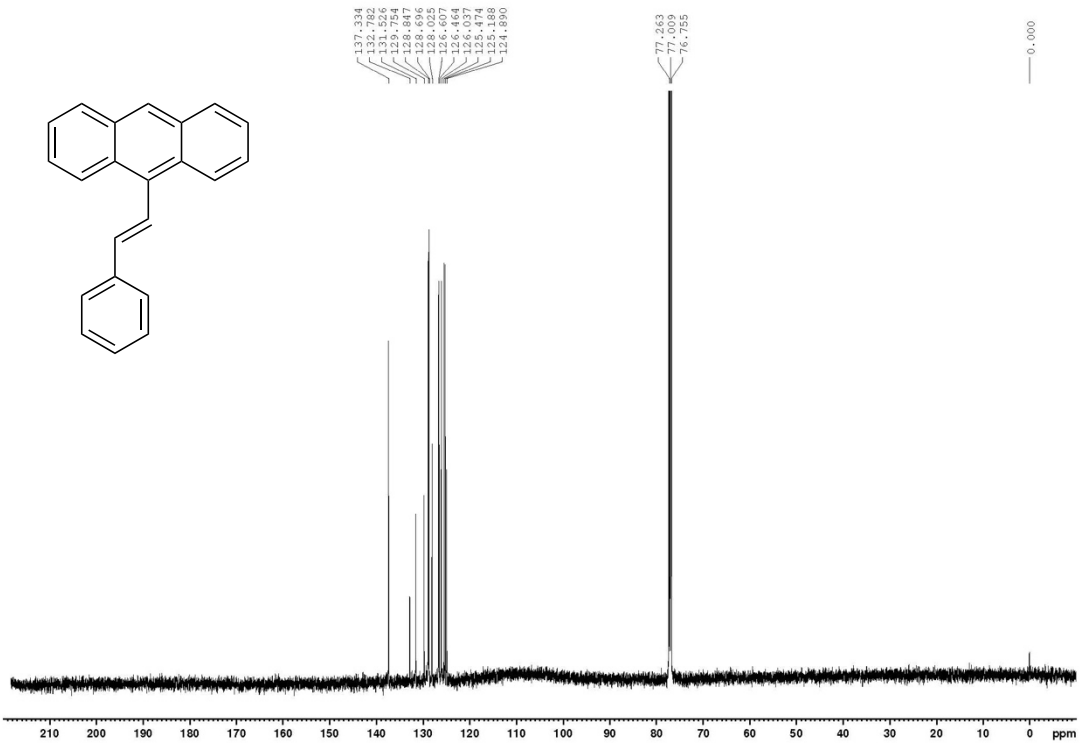
8.047
8.046
8.045
8.030
8.029
8.028
7.718
7.714
7.705
7.701
7.630
7.628
7.612
7.610
7.472
7.470
7.459
7.457
7.453
7.442
7.440
7.373
7.371
7.360
7.358
7.356
7.353
7.343
7.340
7.311
7.307
7.298
7.295
7.290
7.282
5.283
1.522
0.000
Br
1.00
2.00
2.01
2.00
2.12
2.06
2.12
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

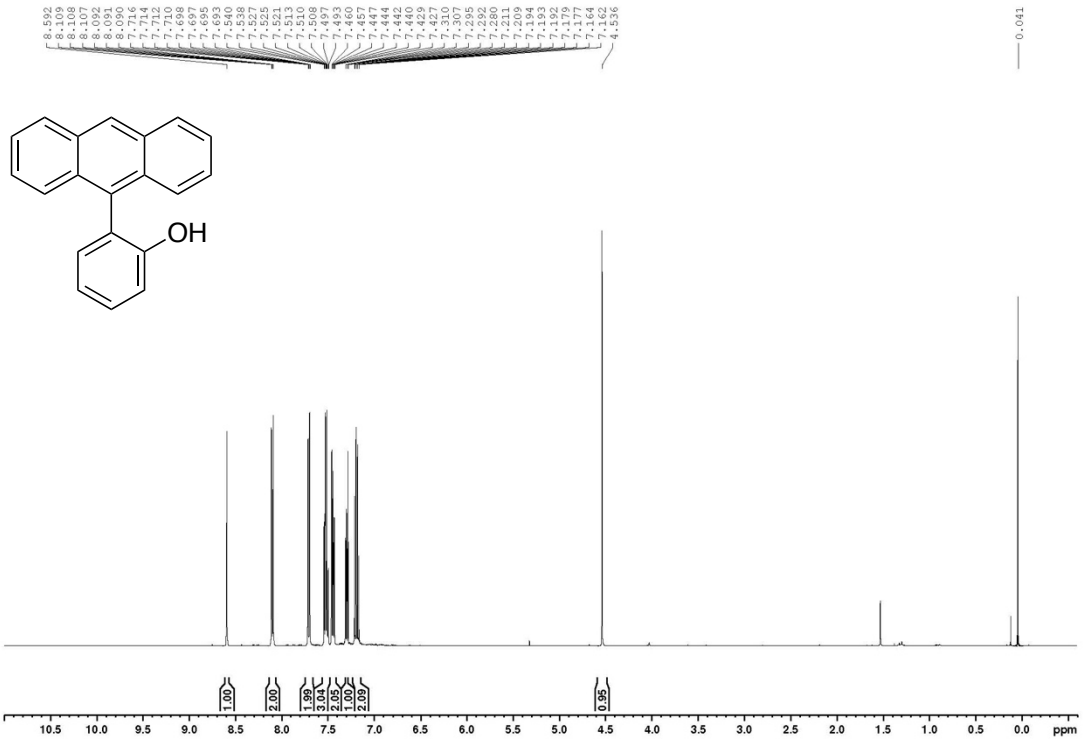

137.719
135.424
132.954
131.619
131.287
130.043
128.411
126.960
126.407
125.609
125.162
121.716
77.256
76.749
0.004
Br
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

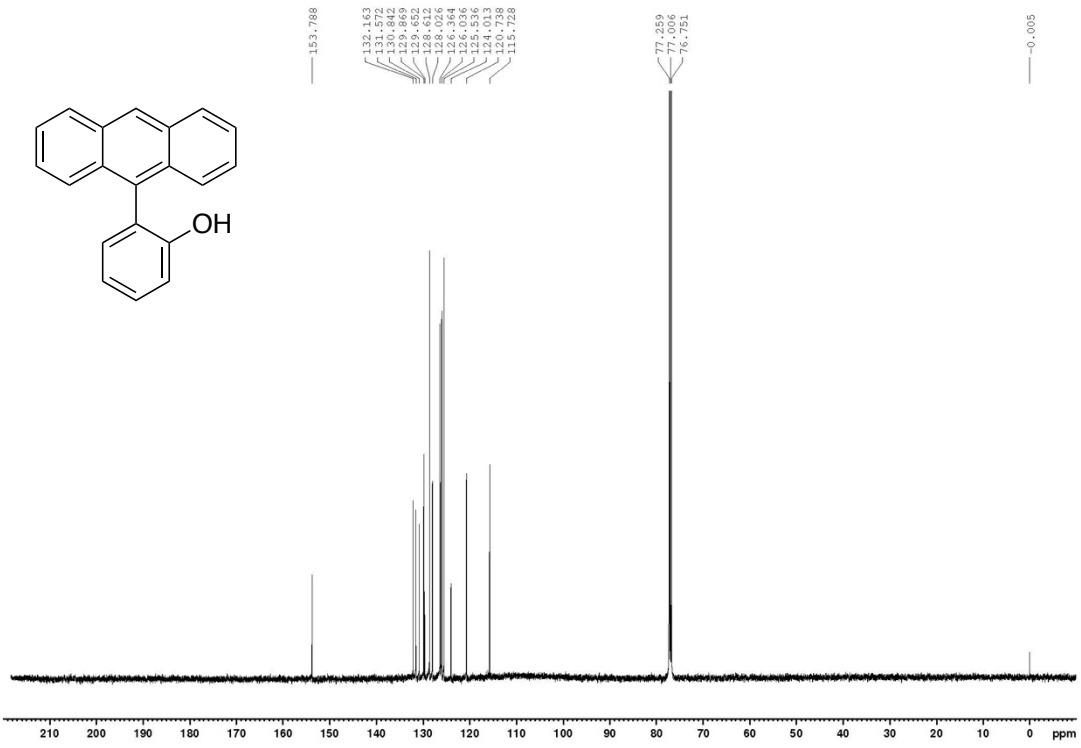

8.578
8.094
8.077
8.052
8.036
8.001
7.985
7.692
7.678
7.675
7.661
7.525
7.523
7.511
7.509
7.477
7.475
7.464
7.461
7.458
7.456
7.454
7.447
7.443
7.441
7.439
7.437
7.426
7.424
7.402
7.400
7.384
7.382
7.250
7.248
7.245
7.237
7.235
7.232
7.230
7.220
7.217
7.194
7.192
7.181
7.178
7.175
7.164
7.161
7.071
7.069
7.054
7.052
5.286
1.520
0.000
1.00
2.02
1.01
1.01
1.04
1.02
3.05
2.03
2.51
1.12
1.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

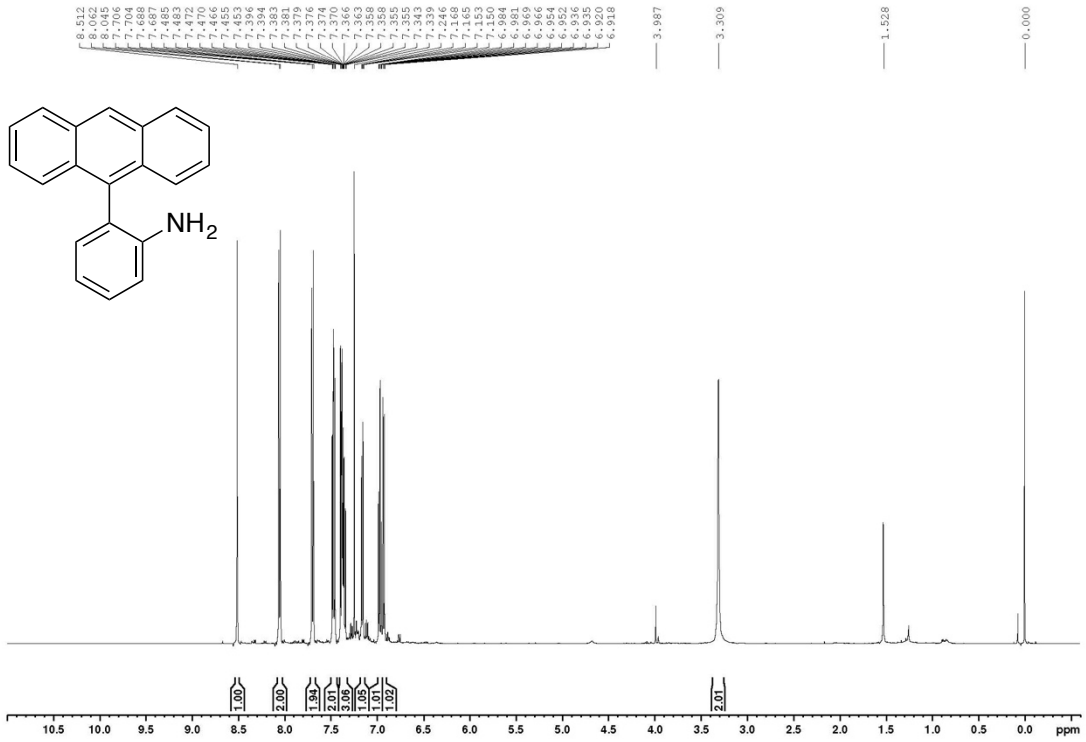

136.482
134.924
133.667
133.484
131.394
130.972
129.078
128.374
128.187
128.076
126.899
126.678
126.534
126.207
125.943
125.527
125.471
125.164
77.257
77.003
76.749
0.005
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

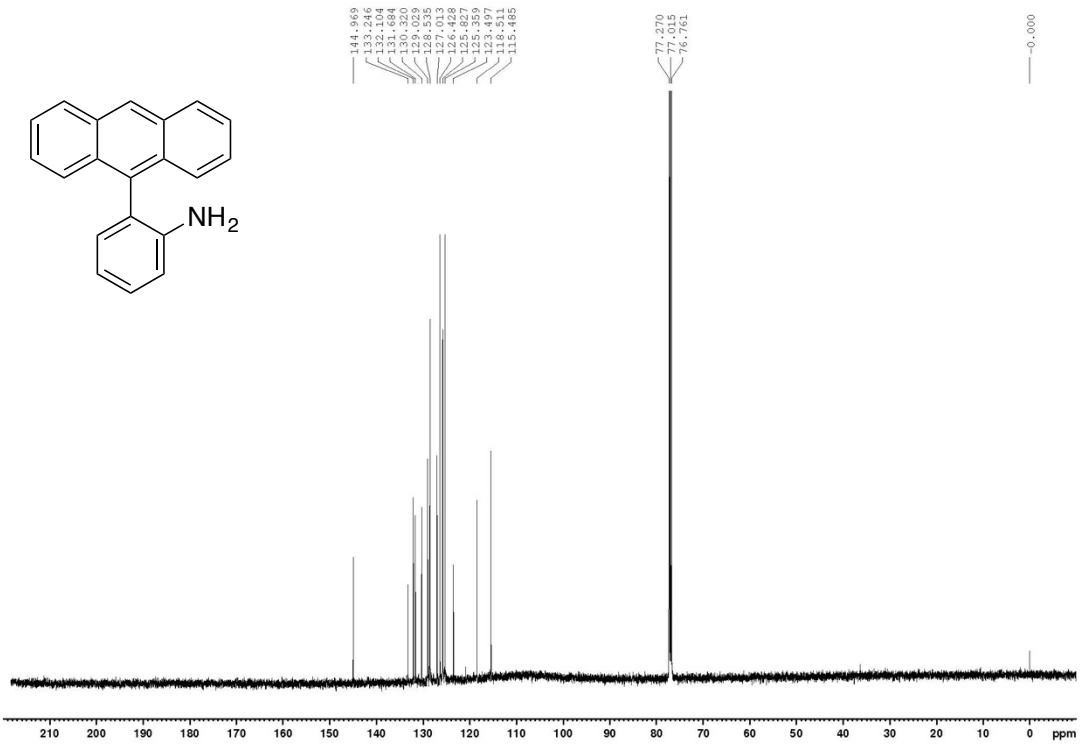

8.369
8.367
8.365
8.362
8.360
8.356
8.354
8.352
8.351
8.349
8.347
8.025
8.019
8.018
8.013
8.013
8.006
8.005
7.938
7.937
7.905
7.904
7.692
7.691
7.689
7.688
7.685
7.675
7.674
7.673
7.493
7.489
7.480
7.476
7.474
7.467
7.460
7.457
7.454
7.444
7.441
7.376
7.377
7.371
7.362
7.359
7.355
7.344
7.248
6.972
6.939
1.523
0.000
1.00
1.99
2.00
1.04
2.04
6.03
0.98
1.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

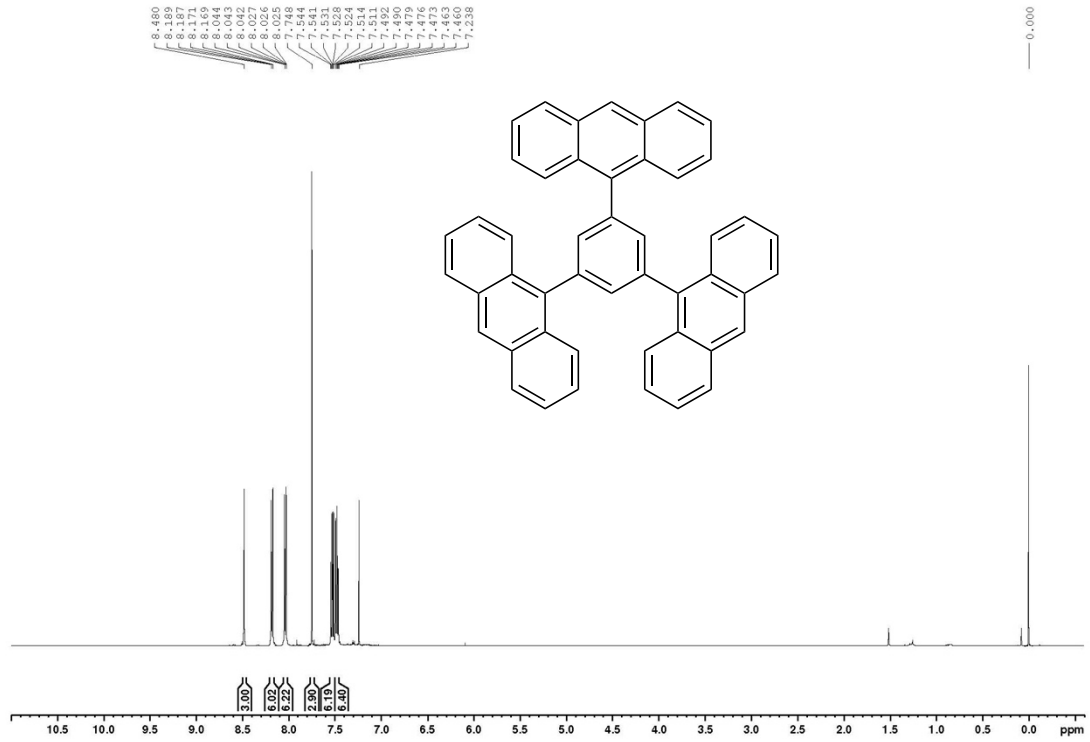

137.334
132.782
131.526
129.754
128.847
128.696
128.025
126.607
126.464
126.037
125.474
125.188
124.890
77.263
77.009
76.755
0.000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

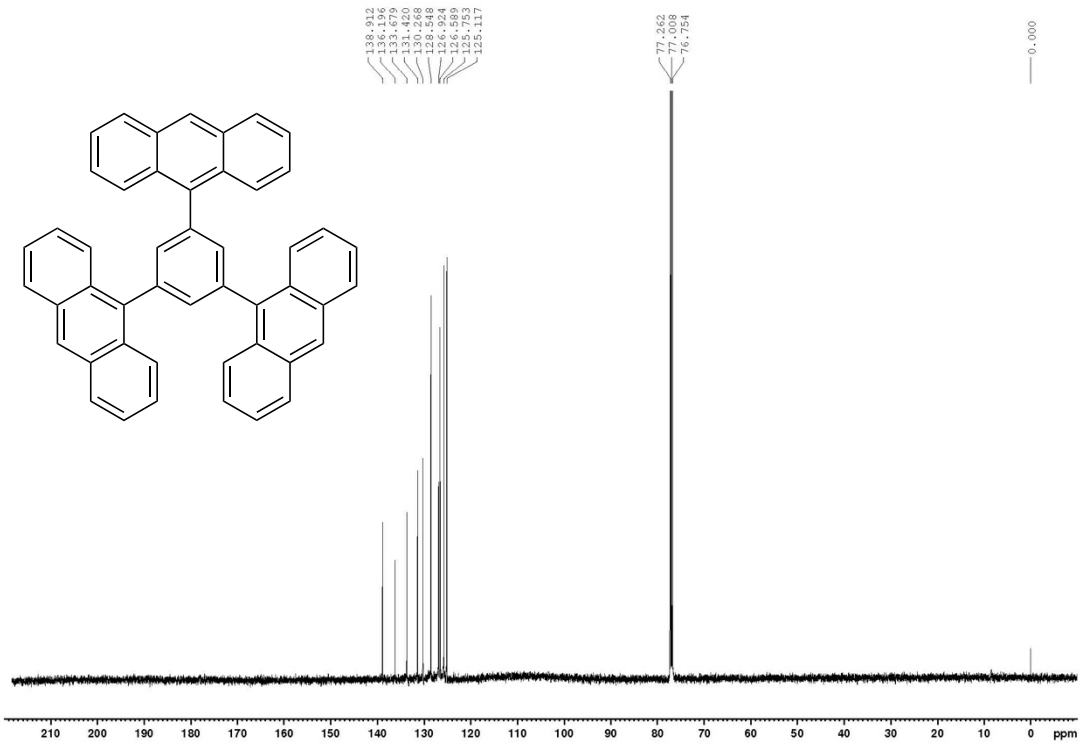

OH
1.00
2.00
1.98
3.04
2.05
1.00
2.09
0.96
ppm

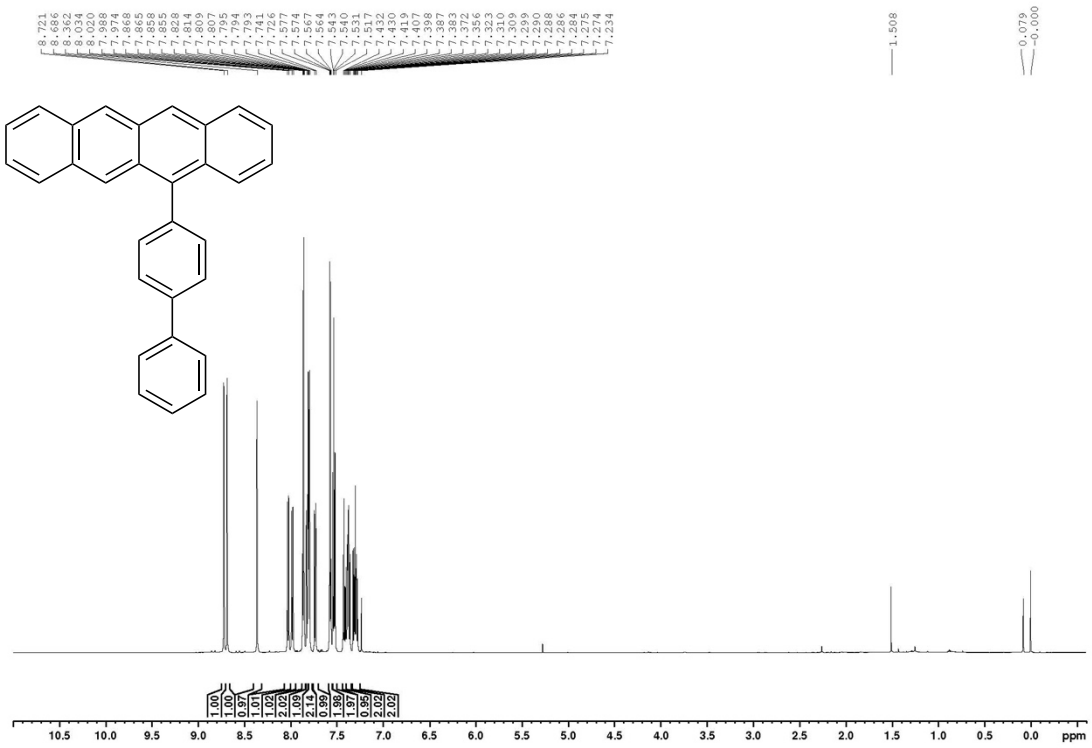

OH
153.788
132.163
131.572
130.842
130.469
129.652
128.612
128.026
126.364
126.036
125.536
124.013
120.738
115.728
77.259
77.006
76.751
-0.005
ppm


8.512
8.062
8.045
7.706
7.704
7.688
7.687
7.485
7.483
7.472
7.470
7.466
7.455
7.453
7.396
7.394
7.383
7.381
7.379
7.376
7.374
7.370
7.366
7.363
7.358
7.355
7.355
7.343
7.339
7.246
7.168
7.165
7.153
7.150
6.984
6.981
6.969
6.966
6.954
6.952
6.936
6.935
6.920
6.918
3.987
3.309
1.528
0.000
NH2
1.00
2.00
1.94
2.01
3.06
1.05
1.01
1.02
2.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


144.969
133.246
132.104
131.684
131.320
129.029
128.535
127.013
126.428
125.827
125.359
123.497
123.411
115.485
77.270
77.015
76.761
0.000
NH2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.480
8.189
8.187
8.171
8.169
8.044
8.043
8.042
8.027
8.026
8.025
7.548
7.544
7.541
7.531
7.528
7.524
7.514
7.511
7.492
7.490
7.479
7.476
7.473
7.463
7.460
7.238
0.000
3.00
6.02
6.22
2.90
6.19
6.40
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


138.912
136.196
133.679
131.420
130.268
128.548
126.924
126.589
125.753
125.117
77.262
77.008
76.754
0.000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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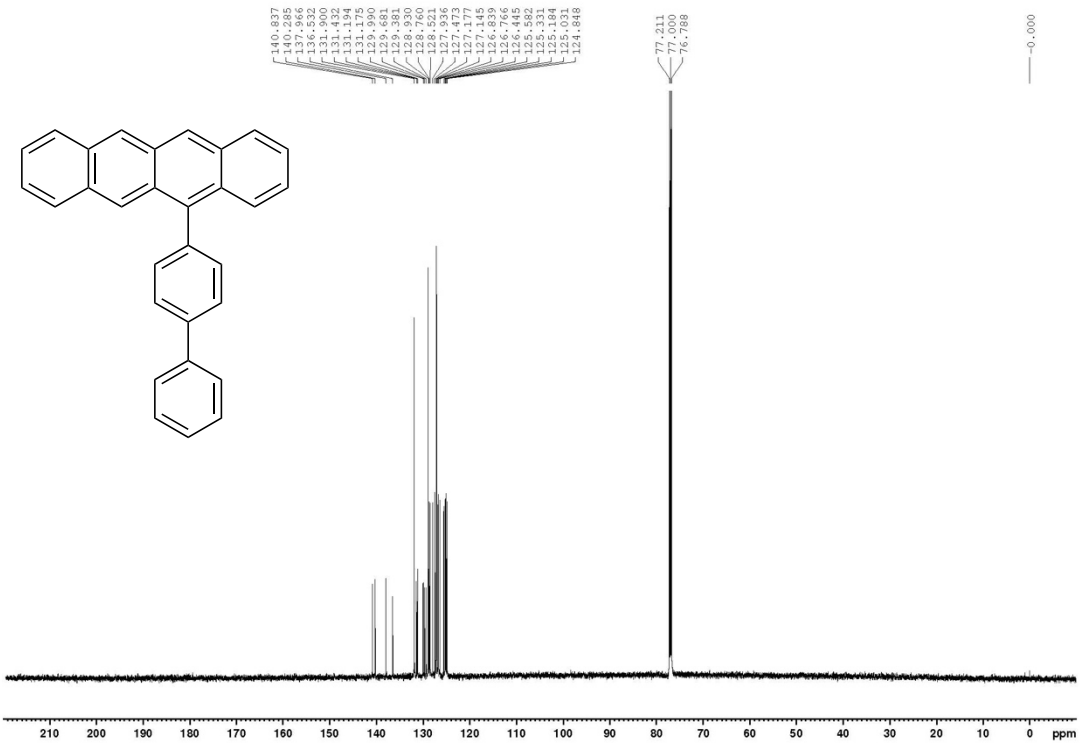
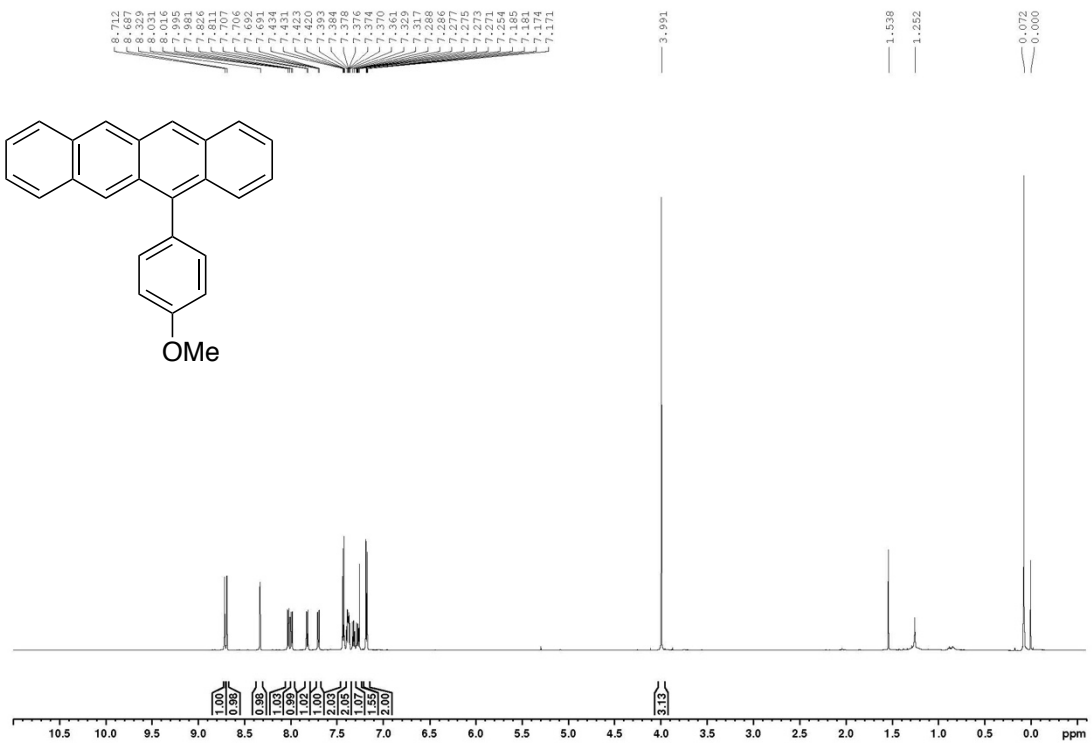
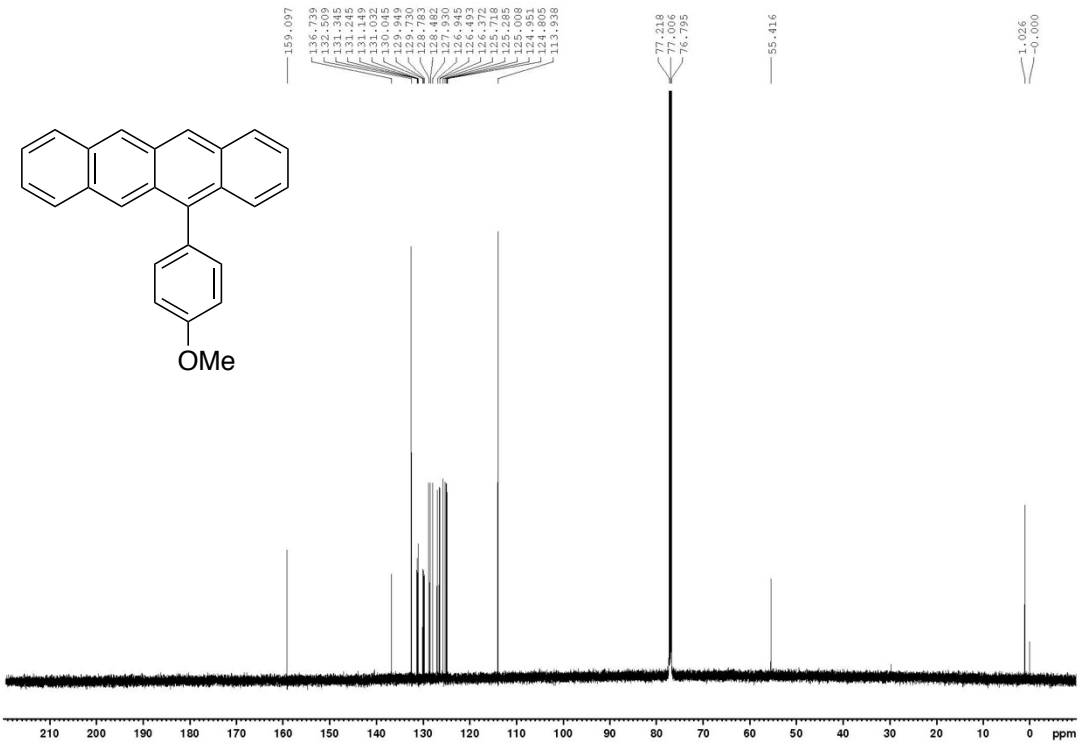
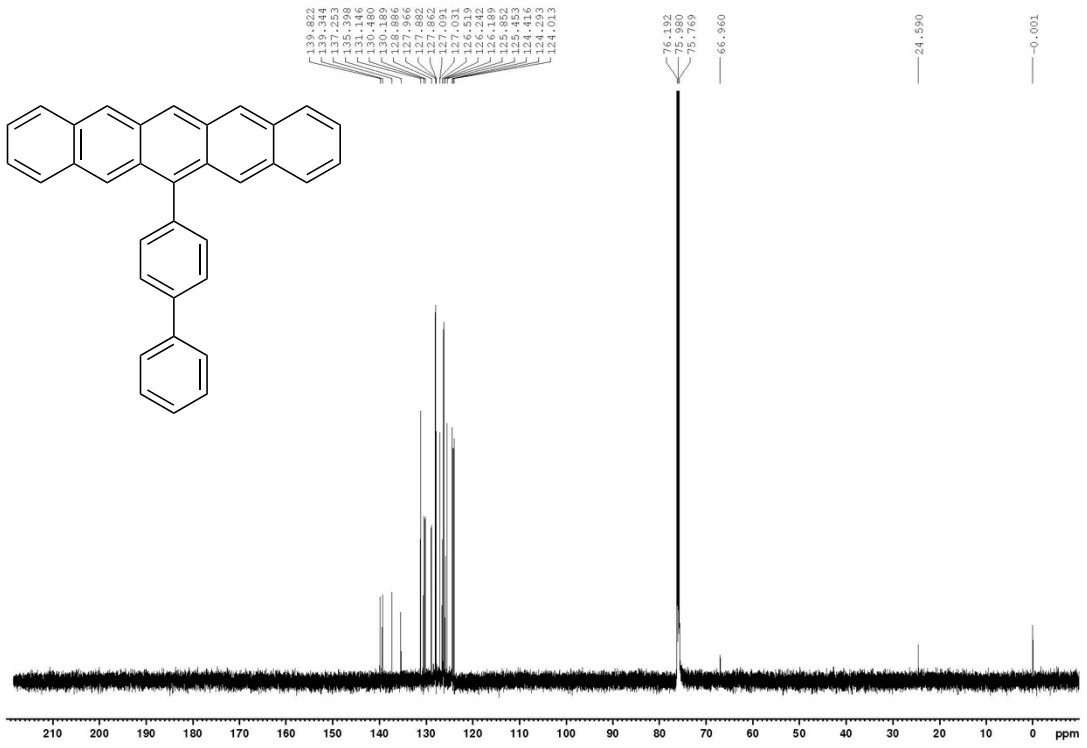
8.686
8.352
8.034
8.020
7.988
7.974
7.868
7.865
7.858
7.855
7.828
7.814
7.809
7.807
7.795
7.794
7.783
7.741
7.726
7.577
7.574
7.567
7.564
7.543
7.540
7.531
7.517
7.432
7.430
7.419
7.407
7.398
7.387
7.383
7.372
7.356
7.323
7.310
7.309
7.299
7.290
7.288
7.286
7.284
7.275
7.274
7.234
1.508
0.079
-0.000
1.00
1.00
0.97
1.01
1.02
2.02
1.09
2.14
0.99
1.88
1.97
0.95
2.02
2.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

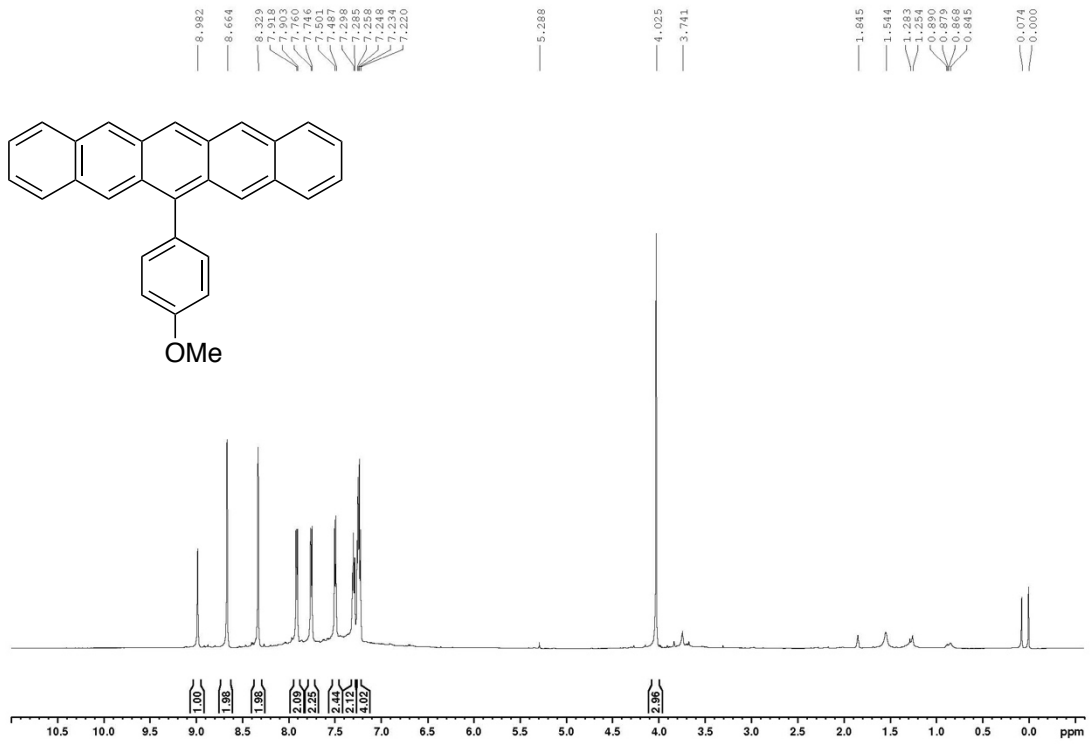

140.837
140.285
137.966
136.532
131.900
131.432
131.194
131.175
129.990
129.681
129.381
128.930
128.760
128.521
127.936
127.473
127.177
127.145
126.839
126.766
126.445
126.382
125.331
125.184
125.031
124.848
77.211
77.000
76.788
-0.000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

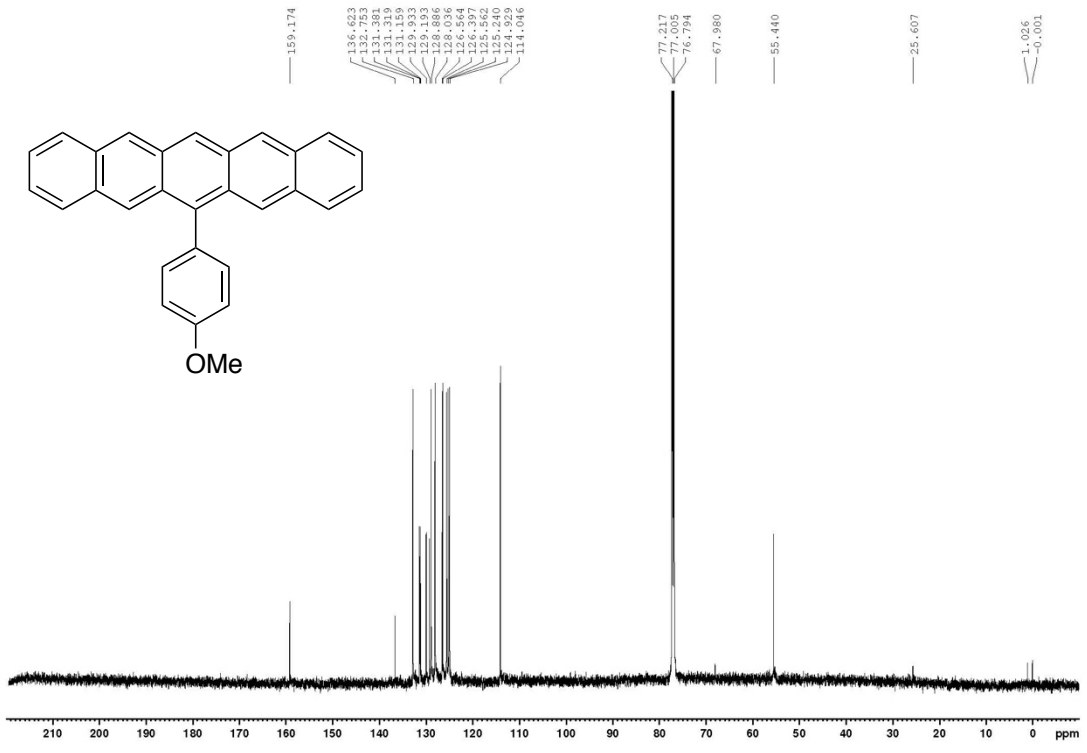

OMe
3.991
1.538
1.252
0.072
0.000
ppm

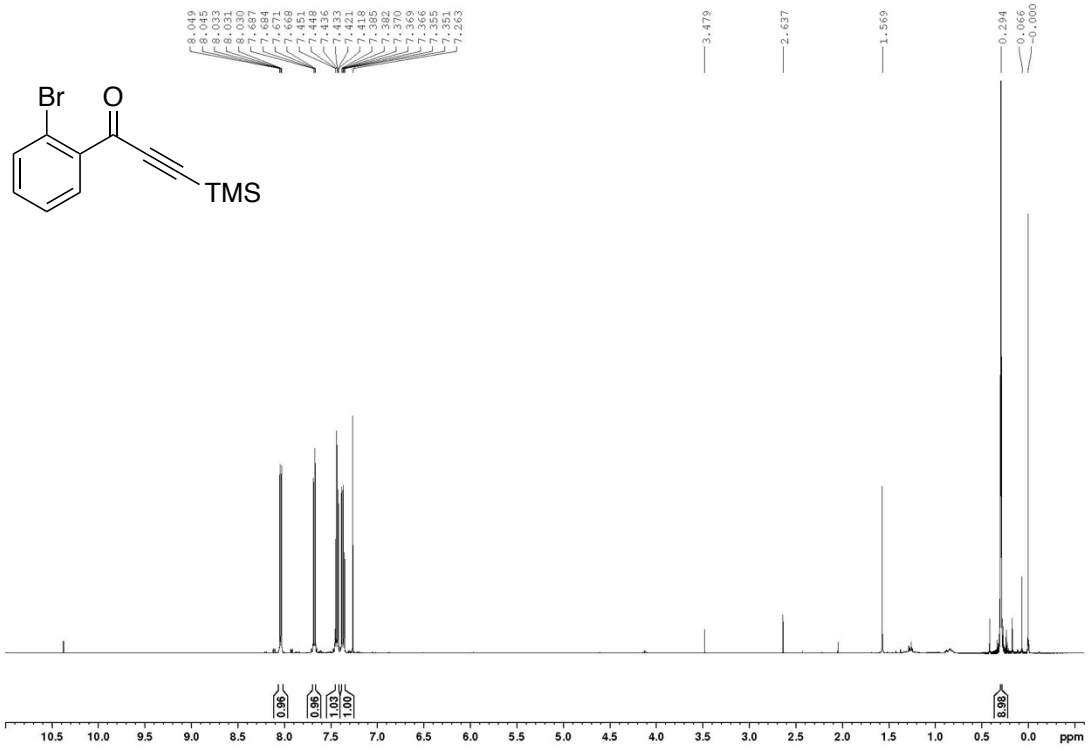

OMe
159.097
136.739
132.509
131.345
131.245
131.149
131.032
130.045
129.949
129.730
128.783
128.482
128.300
127.945
126.493
126.372
125.718
125.285
125.008
124.851
124.805
113.938
77.218
77.006
76.795
55.416
1.026
0.000
ppm

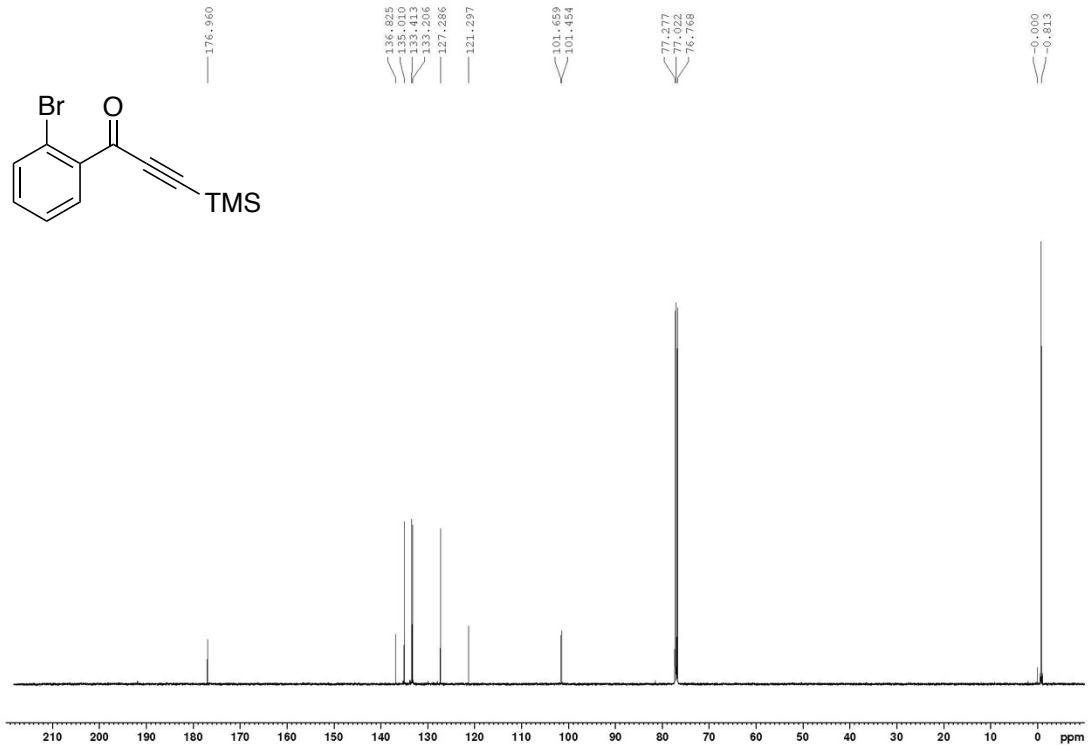

9.053
8.718
8.377
7.952
7.930
7.939
7.936
7.876
7.864
7.783
7.769
7.660
7.646
7.584
7.571
7.558
7.465
7.453
7.440
7.339
7.318
7.304
7.271
7.257
7.247
3.745
1.851
1.533
0.071
0.000
1.00
2.03
2.04
4.12
2.12
2.21
2.21
2.28
1.76
2.42
1.36
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

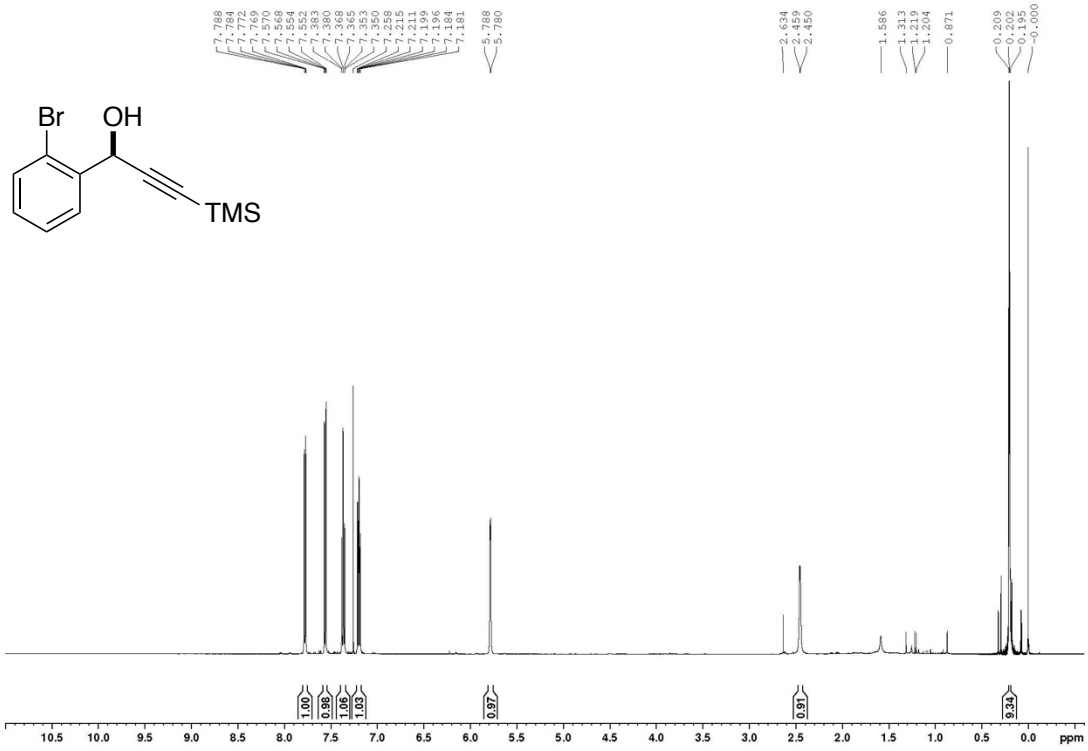

139.822
139.344
137.253
135.398
131.146
130.480
130.189
128.886
128.366
127.882
127.862
127.091
127.031
126.519
126.242
126.189
125.852
125.453
124.416
124.293
124.013
76.192
75.980
75.769
66.960
24.590
-0.001
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

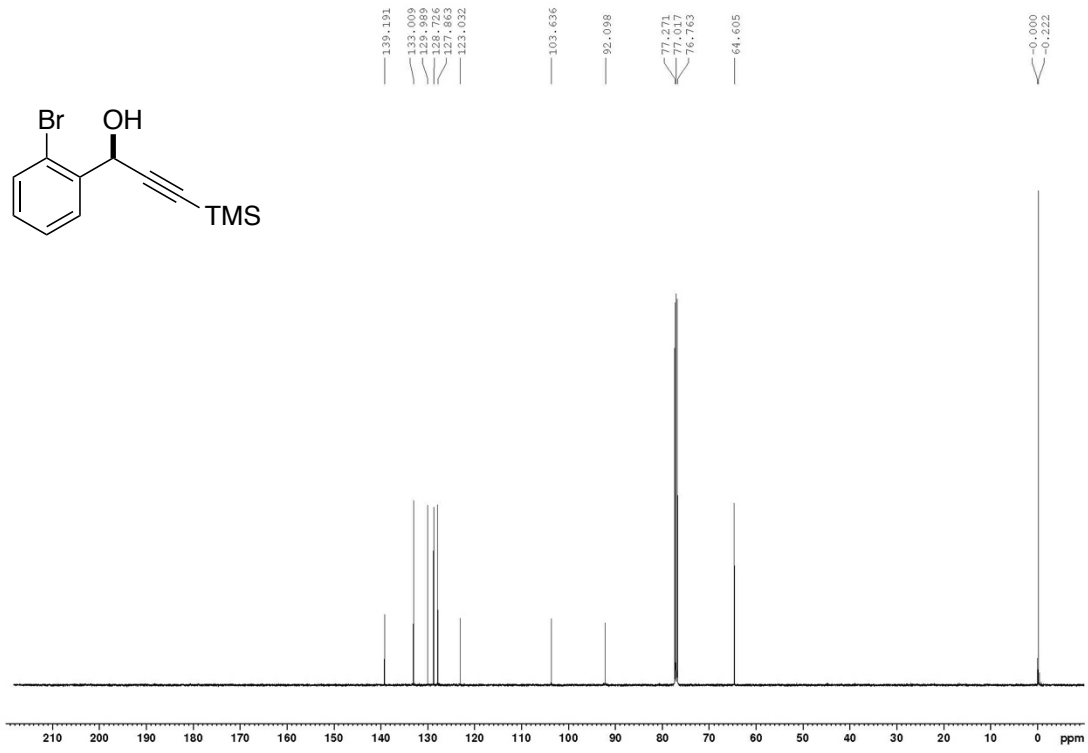

8.982
8.664
8.329
7.918
7.903
7.760
7.746
7.501
7.497
7.288
7.285
7.258
7.248
7.234
7.220
5.288
4.025
3.741
1.845
1.544
1.283
1.234
0.880
0.879
0.868
0.845
0.074
0.000
OMe
1.00
1.98
1.98
2.09
2.25
2.44
2.12
4.02
2.96
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

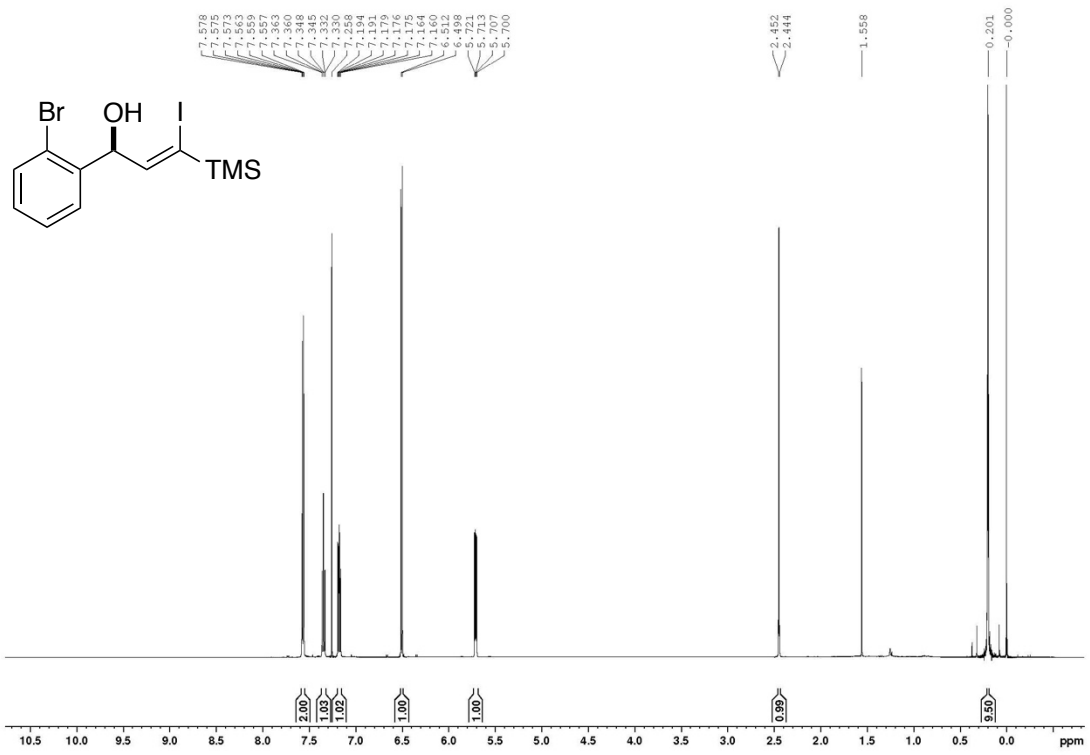

159.174
136.623
132.753
131.381
131.319
131.159
129.933
129.193
128.886
128.036
126.564
126.397
125.562
125.240
124.929
114.046
77.217
77.005
76.794
67.980
55.440
25.607
1.026
-0.001
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

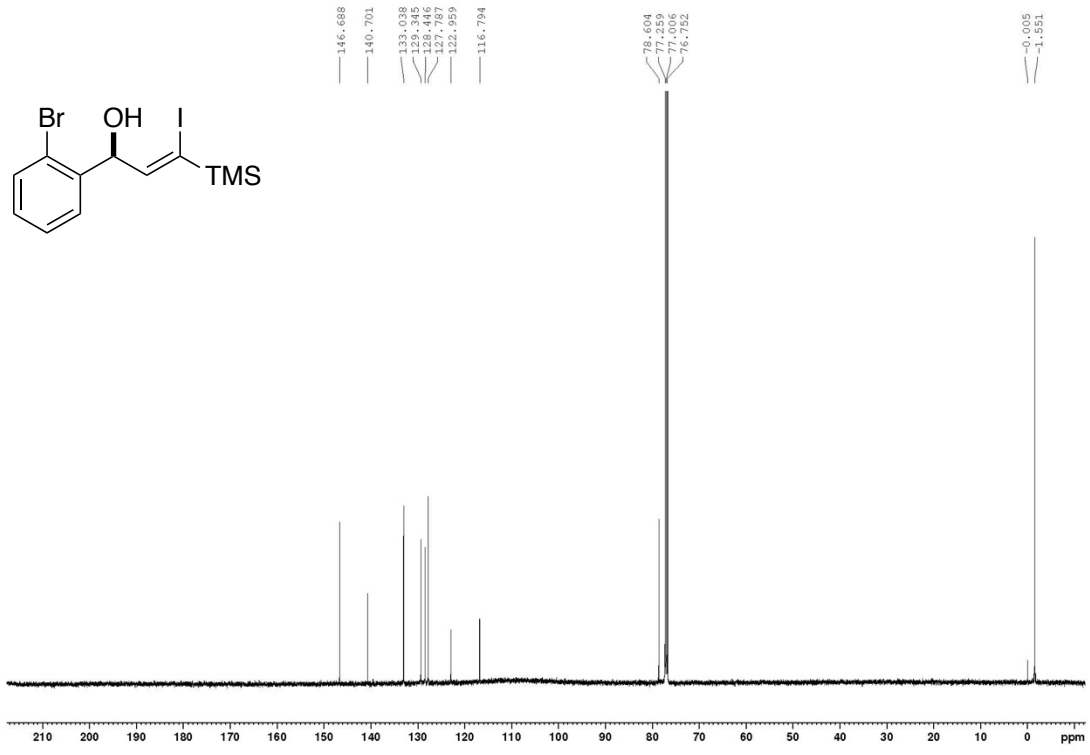

8.049
8.045
8.033
8.031
8.030
8.027
7.684
7.671
7.668
7.451
7.448
7.436
7.433
7.421
7.418
7.385
7.382
7.370
7.369
7.366
7.355
7.351
7.263
3.479
2.637
1.569
0.294
0.066
-0.000
Br
O
TMS
0.96
0.96
1.03
1.00
8.98
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

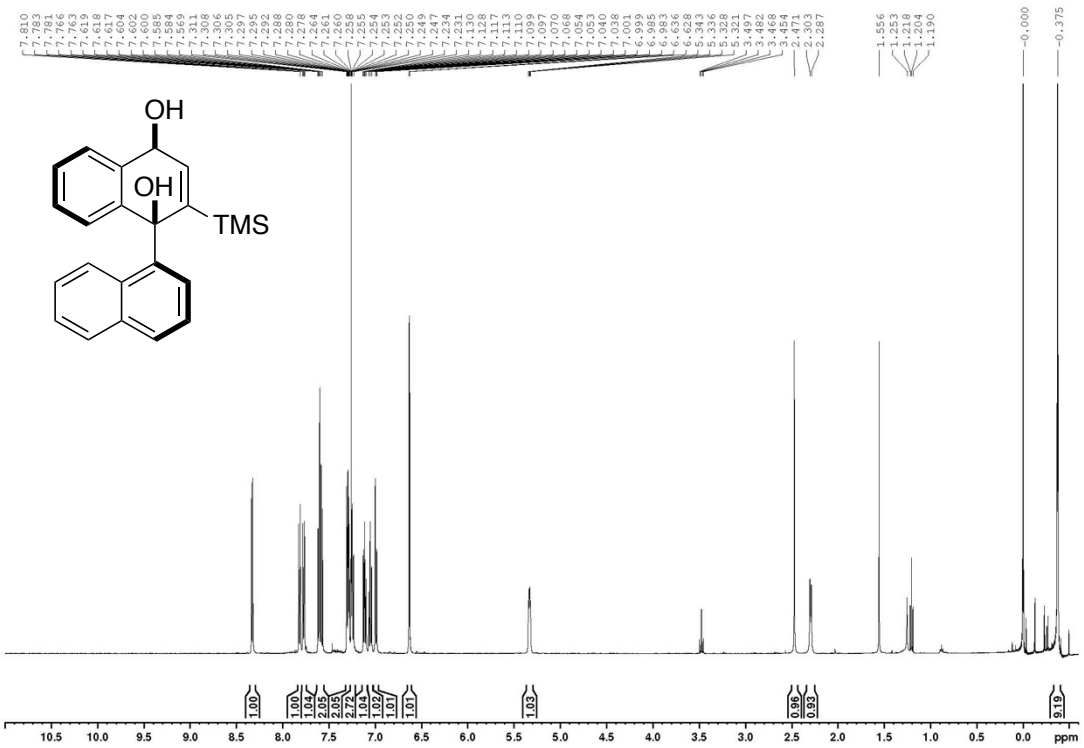

176.960
136.825
135.010
133.413
133.206
127.286
121.297
101.659
101.454
77.277
77.022
76.768
-0.000
-0.813
Br
O
TMS
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

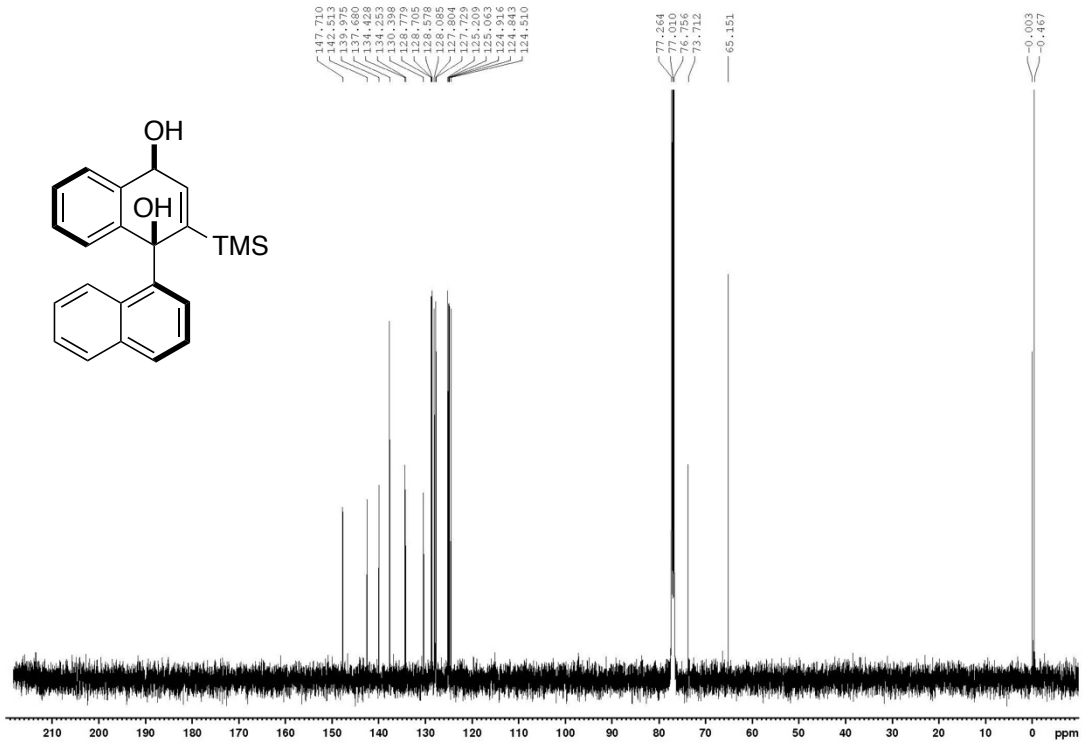

7.788
7.784
7.772
7.769
7.570
7.568
7.554
7.552
7.383
7.380
7.368
7.365
7.353
7.350
7.258
7.215
7.211
7.199
7.196
7.184
7.181
5.788
5.780
2.634
2.459
2.450
1.586
1.313
1.219
1.204
0.871
0.209
0.192
0.185
0.000
Br
OH
TMS
1.00
0.98
1.06
1.03
0.97
0.91
9.34
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

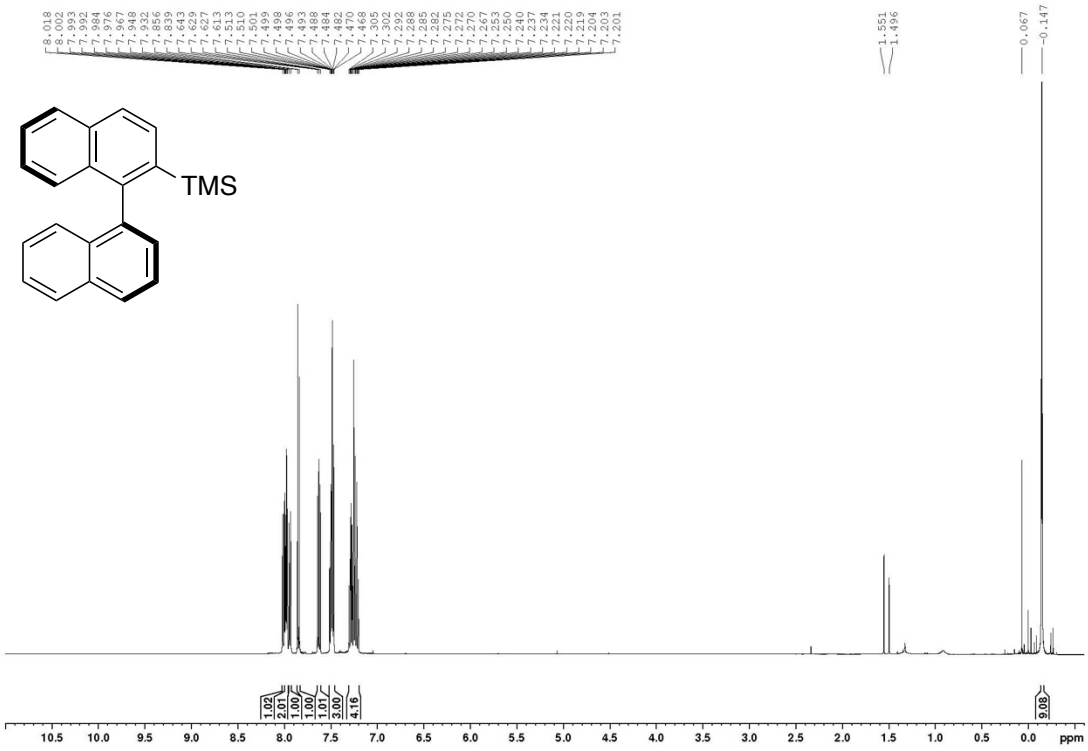

139.191
133.009
129.989
128.726
127.863
123.032
103.636
92.098
77.271
77.017
76.763
64.605
-0.000
-0.222
Br
OH
TMS
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

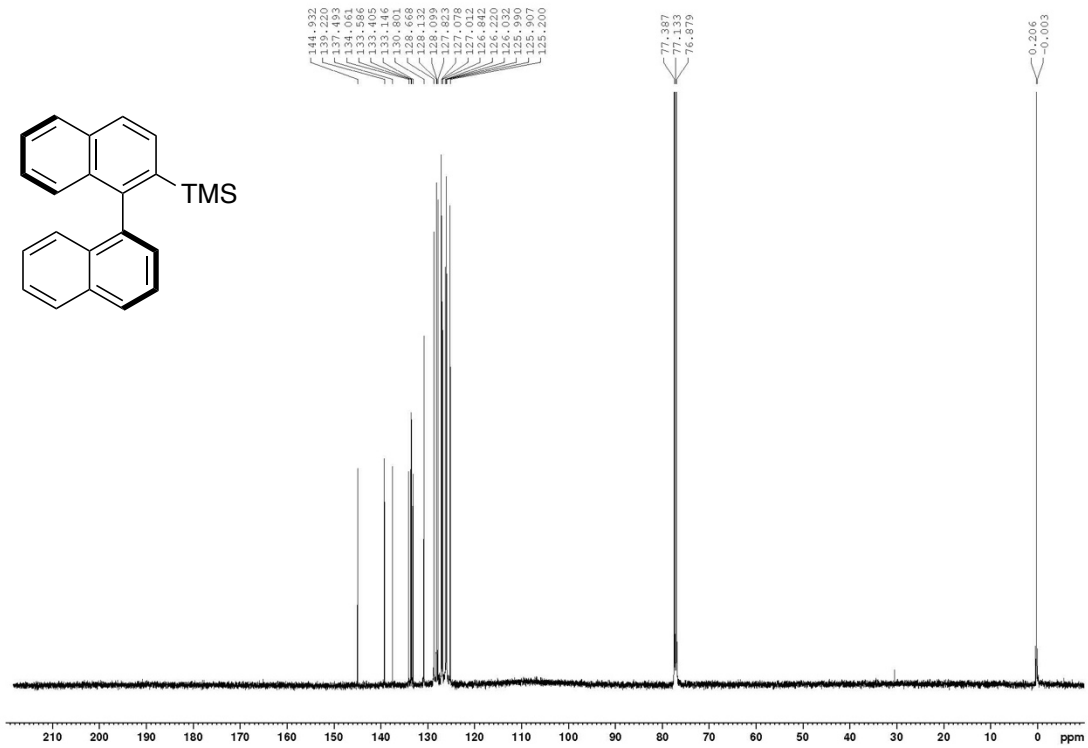

Br
OH
I
TMS
7.578
7.575
7.573
7.563
7.560
7.557
7.363
7.360
7.348
7.345
7.332
7.330
7.258
7.194
7.191
7.179
7.176
7.175
7.164
7.160
6.512
6.498
5.721
5.713
5.707
5.700
2.452
2.444
1.558
0.201
0.000
2.00
1.03
1.02
1.00
1.00
0.99
9.50
ppm

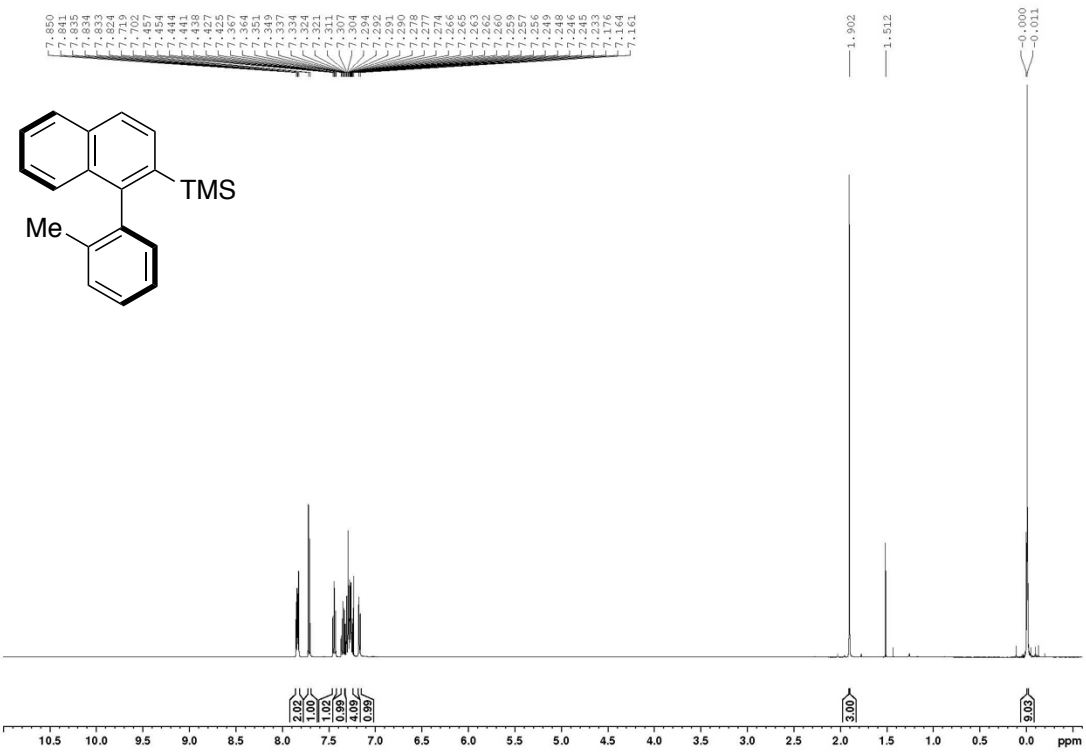

Br
OH
I
TMS
146.688
140.701
133.038
129.345
128.446
127.787
122.959
116.794
78.604
77.259
77.006
76.752
-0.005
-1.551
ppm

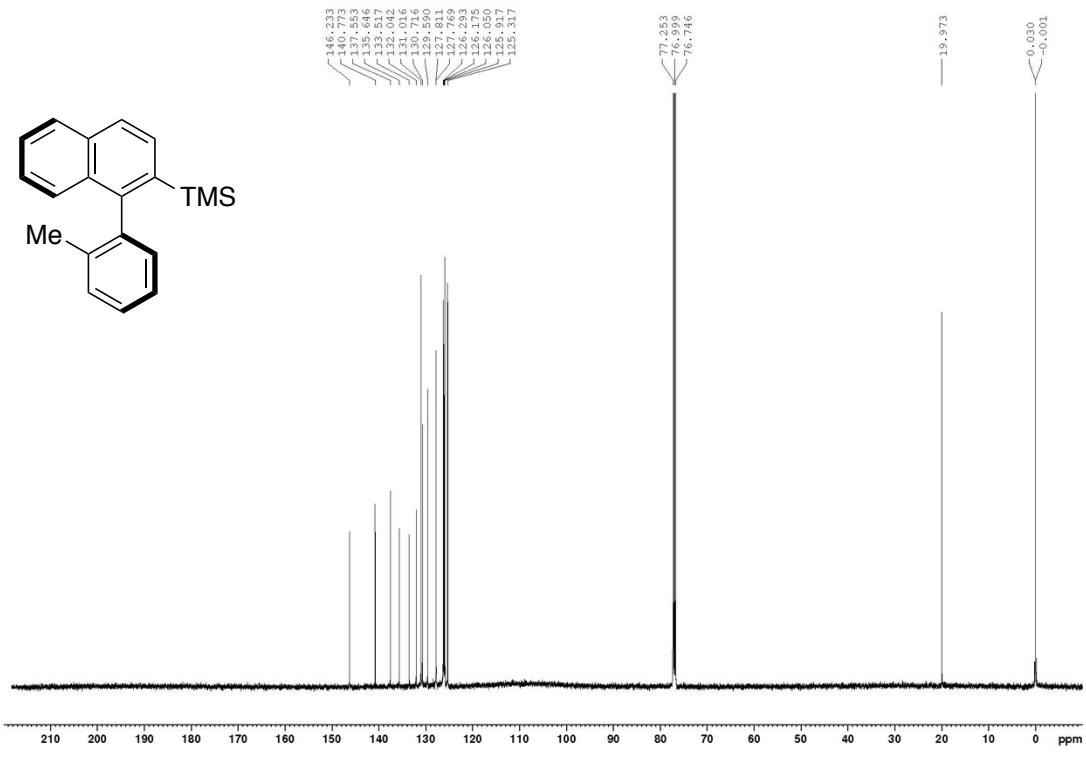

OH
OH
TMS
ppm

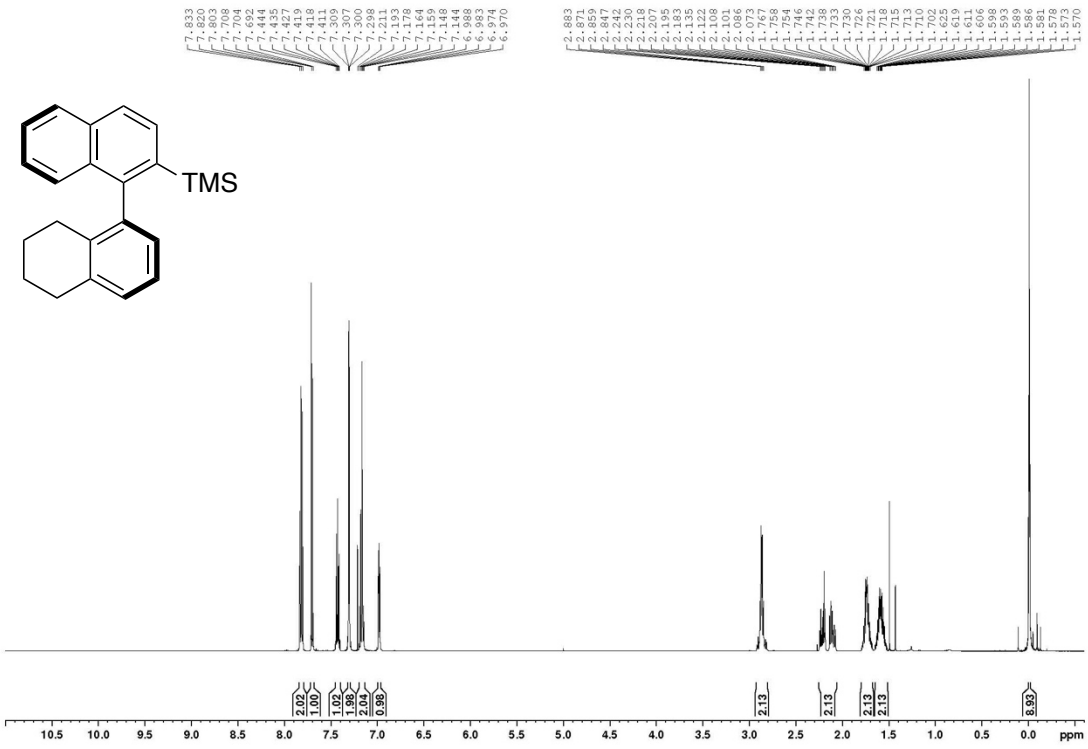

OH
OH
TMS
ppm

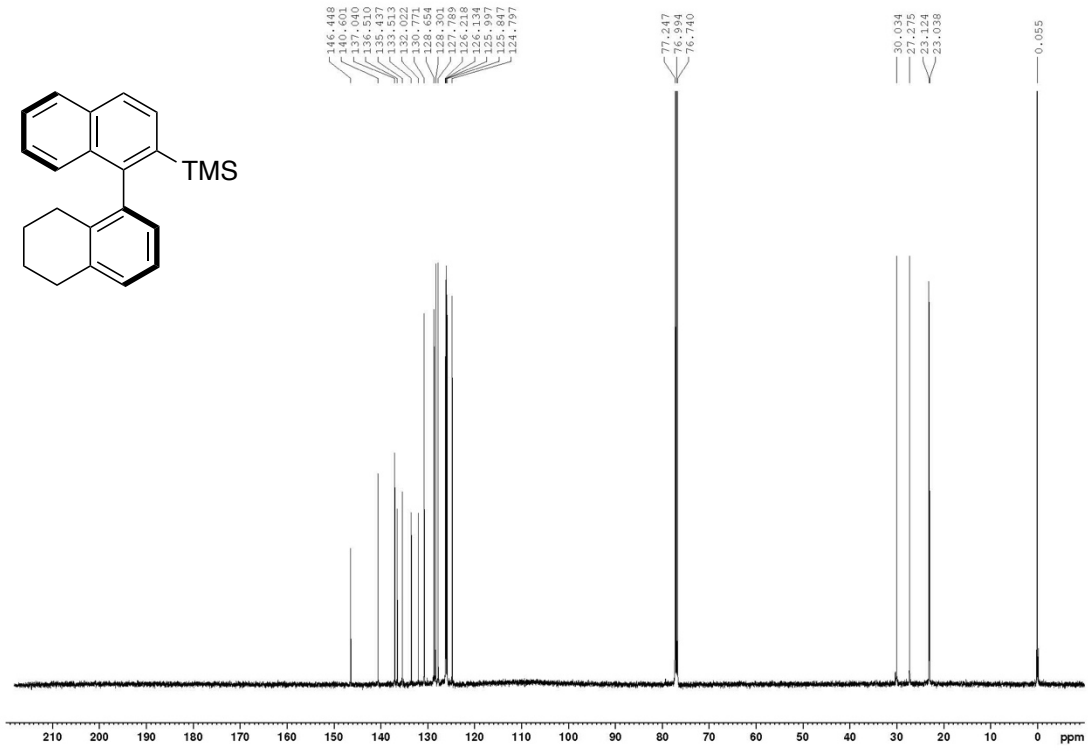

TMS
ppm

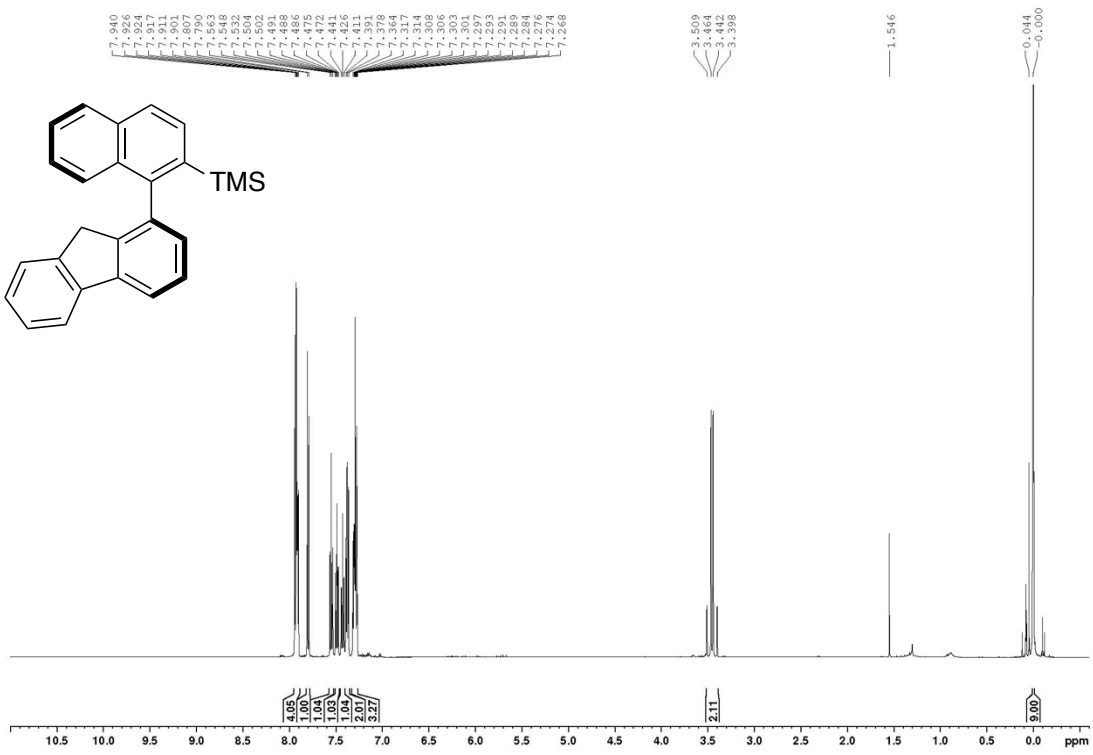

TMS
ppm

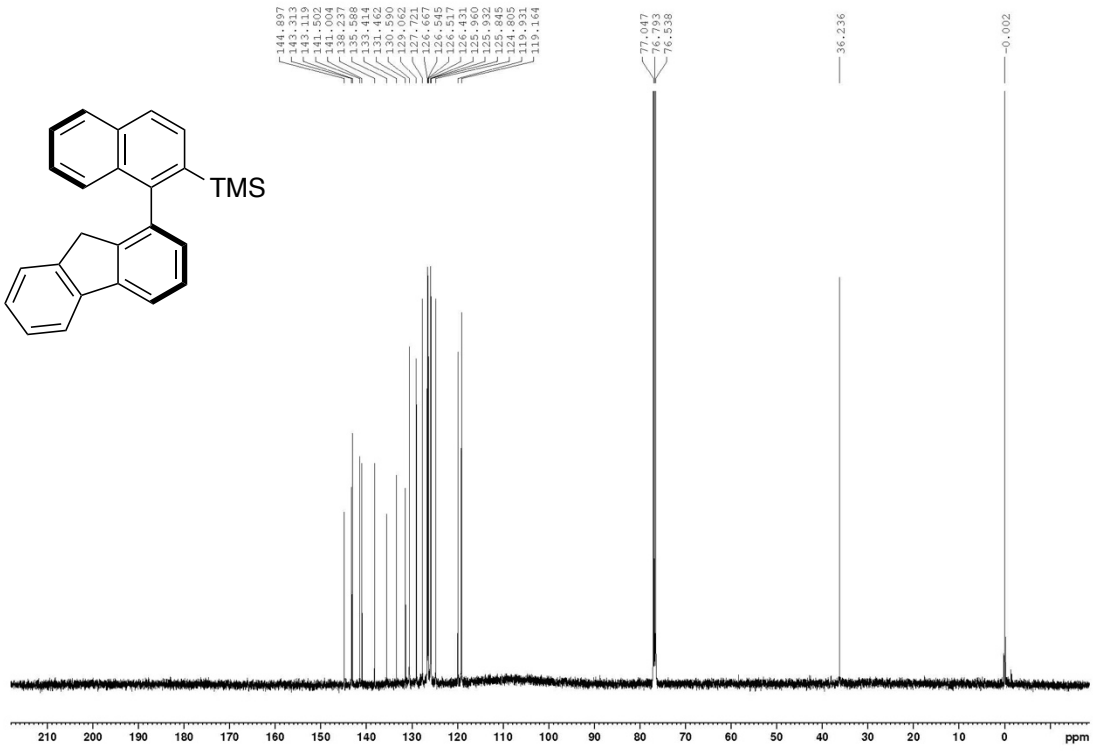

TMS
Me
7.850
7.841
7.835
7.834
7.833
7.824
7.719
7.702
7.457
7.454
7.444
7.441
7.438
7.427
7.425
7.367
7.364
7.351
7.349
7.337
7.334
7.324
7.321
7.311
7.307
7.304
7.294
7.292
7.291
7.290
7.278
7.277
7.274
7.266
7.265
7.263
7.262
7.260
7.259
7.257
7.256
7.249
7.248
7.246
7.245
7.233
7.176
7.164
7.161
1.902
1.512
0.000
-0.011
2.02
1.00
1.02
0.99
4.09
0.99
3.00
9.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

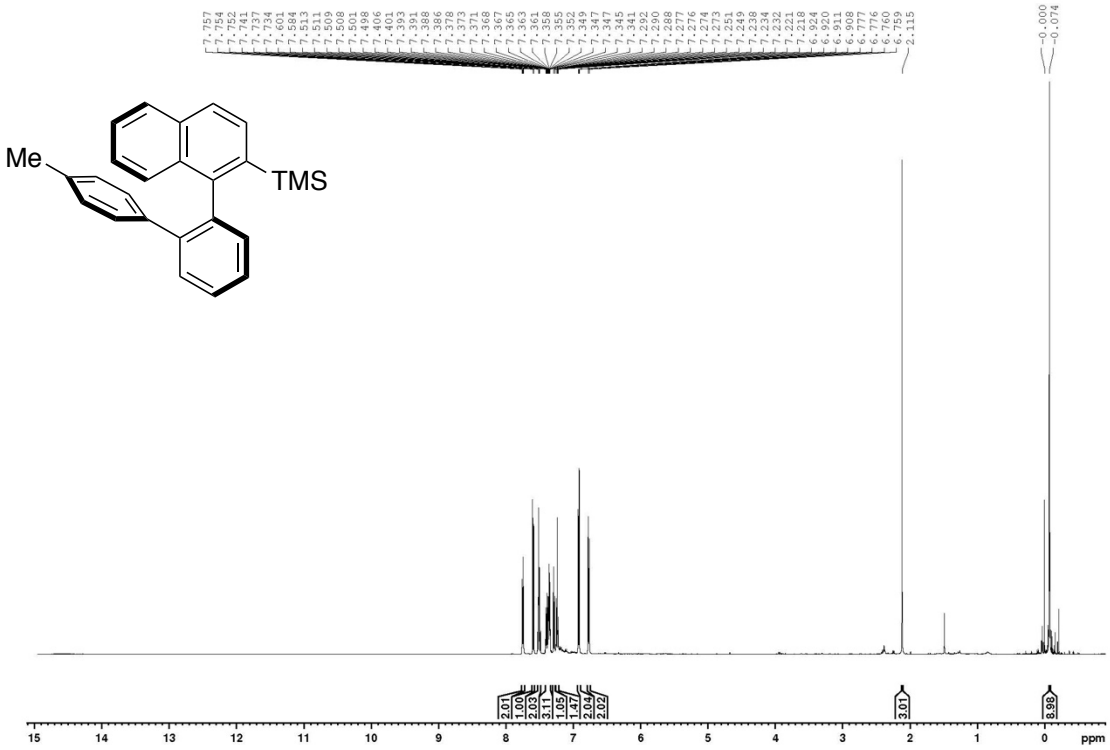

TMS
Me
146.233
140.773
137.553
135.646
133.517
132.042
131.016
130.716
129.590
127.811
127.769
126.293
126.135
126.050
125.917
125.317
77.253
76.999
76.746
19.973
0.030
-0.001
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

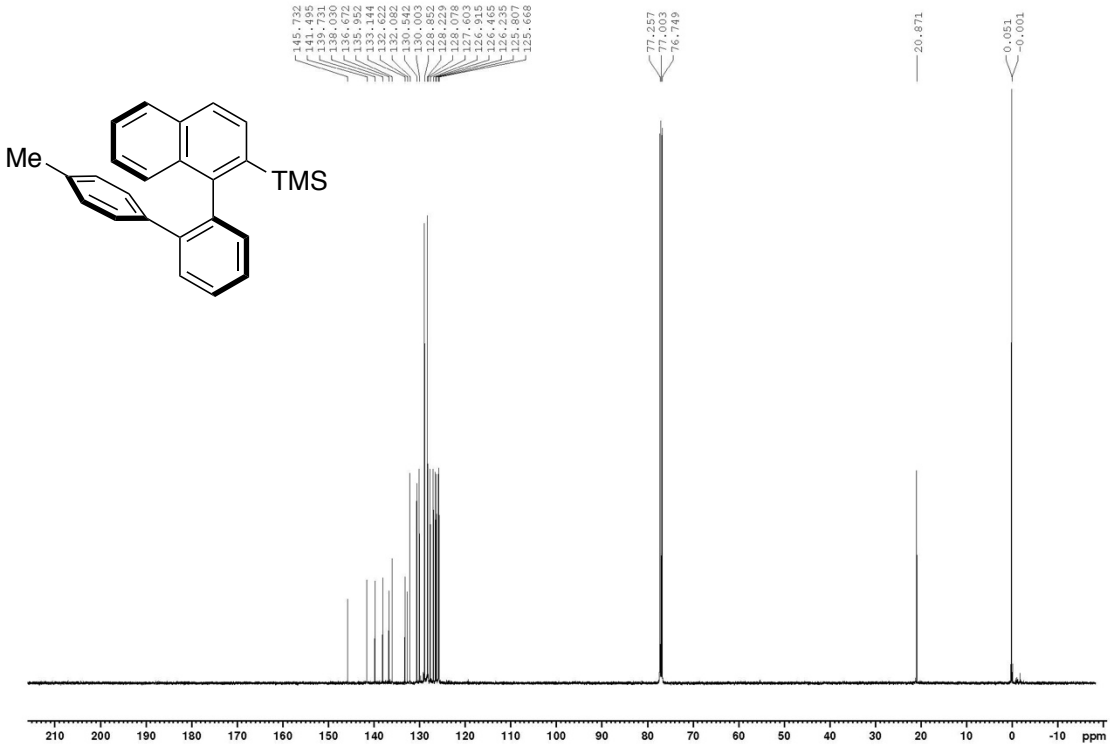

TMS
7.833
7.820
7.803
7.708
7.704
7.692
7.444
7.435
7.427
7.419
7.418
7.311
7.309
7.307
7.300
7.298
7.211
7.193
7.178
7.164
7.159
7.148
7.144
6.988
6.983
6.974
6.970
2.883
2.871
2.859
2.847
2.232
2.230
2.218
2.207
2.195
2.183
2.135
2.122
2.108
2.101
2.086
2.073
1.767
1.758
1.754
1.746
1.742
1.738
1.733
1.730
1.726
1.721
1.718
1.715
1.713
1.710
1.702
1.625
1.619
1.611
1.606
1.598
1.593
1.589
1.586
1.581
1.578
1.573
1.570
2.02
1.00
1.02
1.98
2.04
0.98
2.13
2.13
2.13
2.13
8.93
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

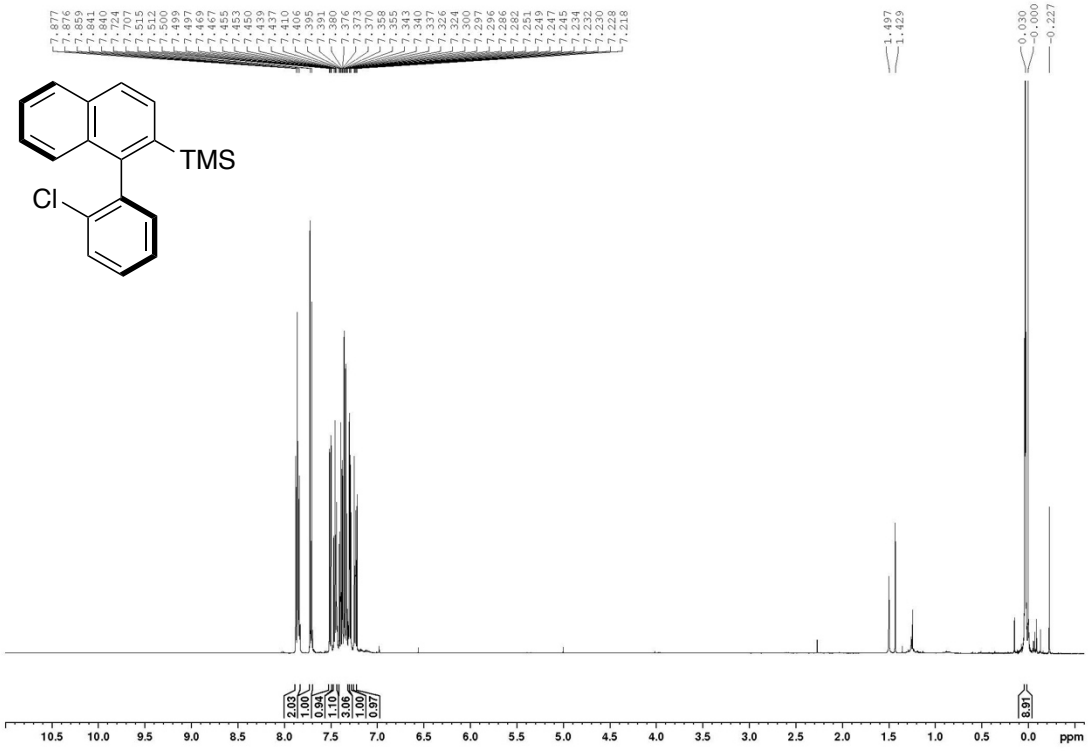

TMS
146.448
140.601
137.040
136.510
135.437
133.153
132.022
130.771
128.654
128.301
127.789
126.218
126.134
125.997
125.847
124.797
77.247
76.994
76.740
30.034
27.125
23.234
23.038
0.055
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

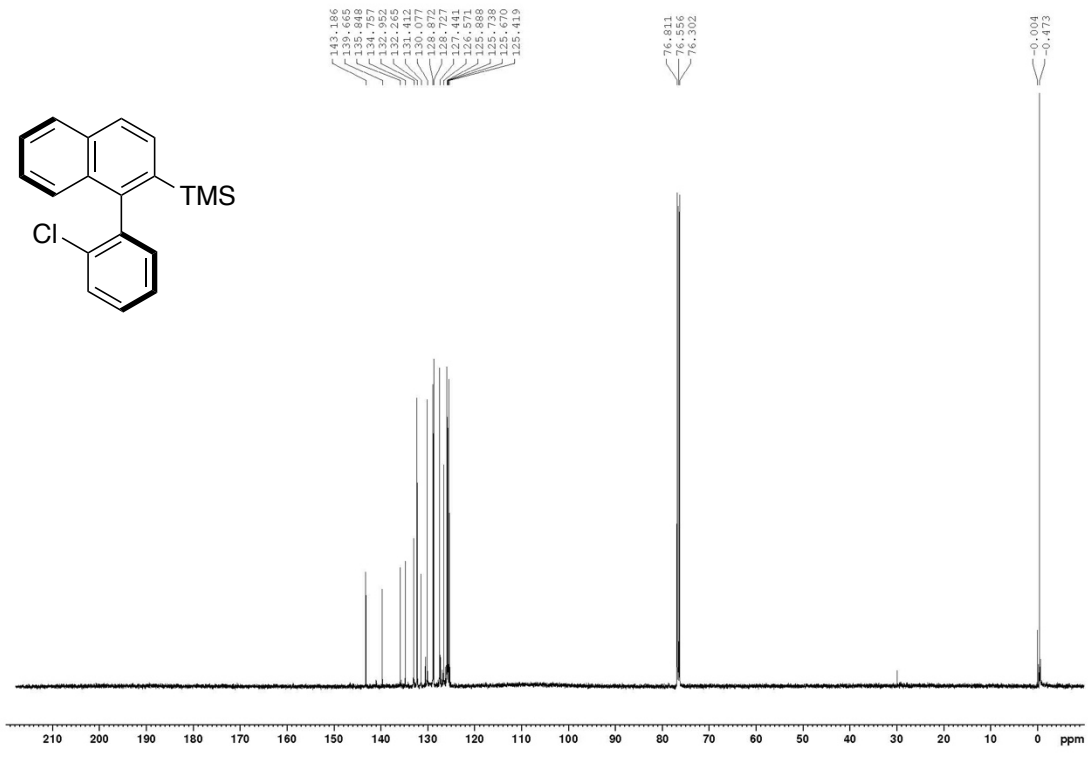

TMS
7.940
7.926
7.924
7.917
7.911
7.901
7.807
7.790
7.563
7.548
7.532
7.504
7.502
7.491
7.488
7.486
7.475
7.472
7.441
7.426
7.411
7.391
7.378
7.364
7.317
7.314
7.308
7.306
7.303
7.301
7.297
7.293
7.291
7.289
7.284
7.276
7.274
7.268
3.509
3.464
3.442
3.398
1.546
0.044
0.000
4.05
1.00
1.04
1.03
1.04
2.01
9.27
2.11
9.00
ppm

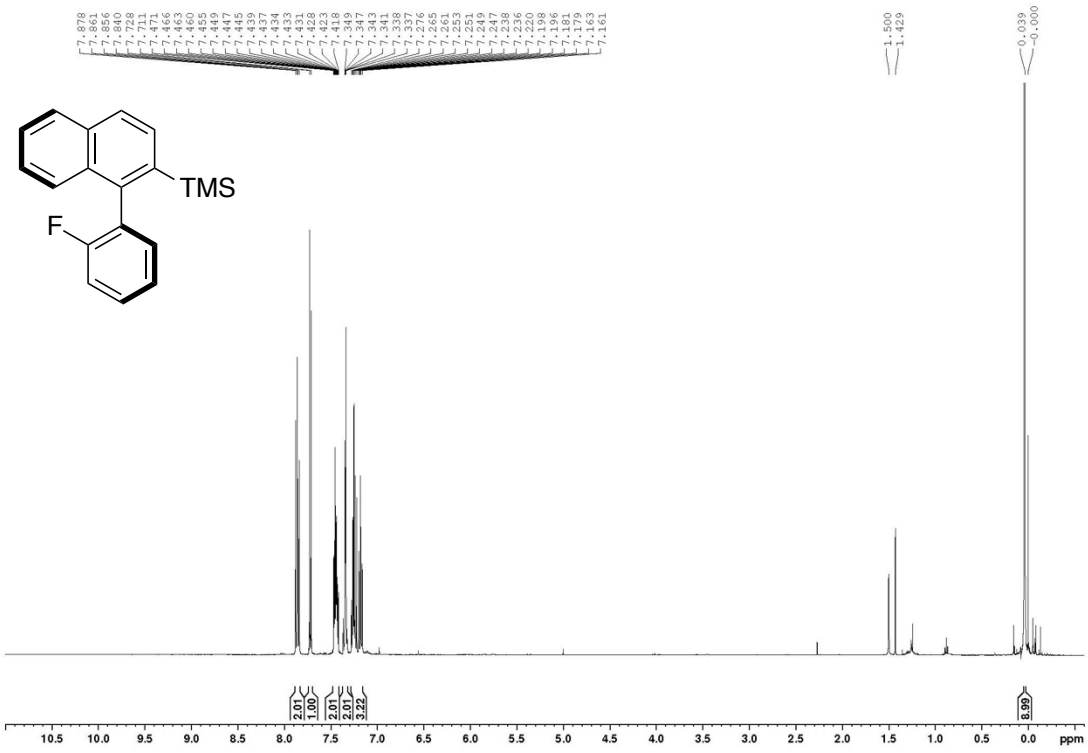

TMS
144.897
143.313
143.119
141.502
141.094
138.237
135.588
133.414
131.462
130.590
129.062
127.721
126.677
126.545
126.517
126.431
125.960
125.932
125.845
124.895
119.931
119.164
77.047
76.793
76.538
36.236
-0.002
ppm

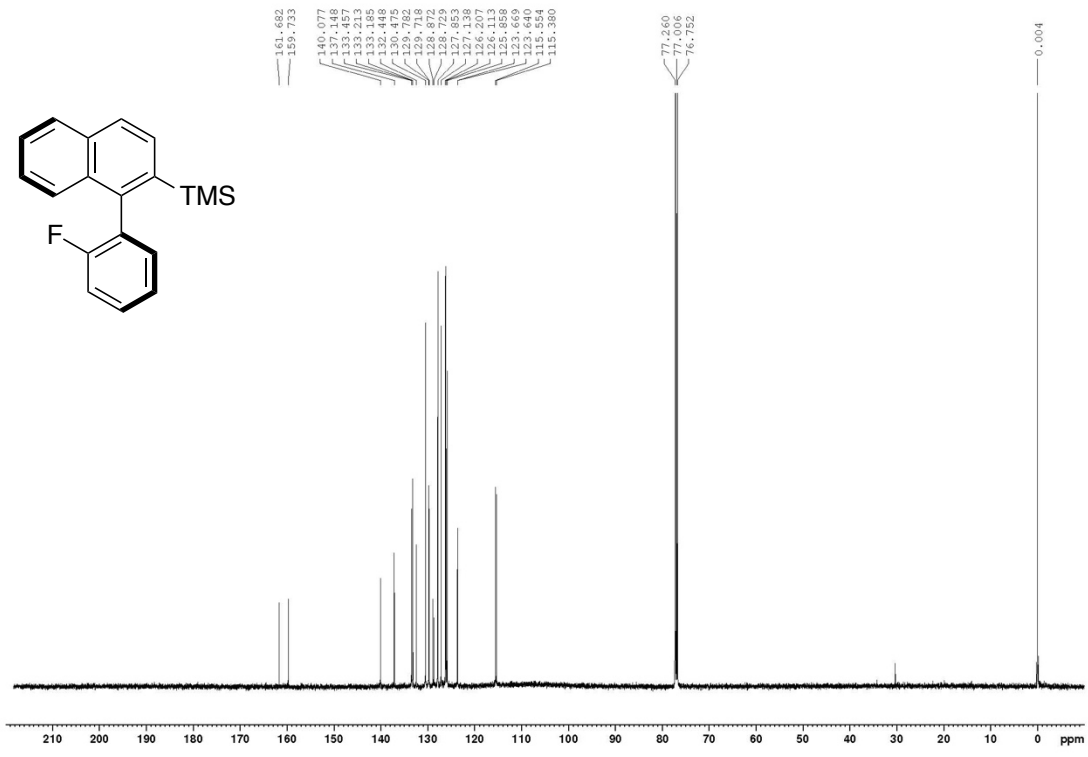

Me
TMS
ppm

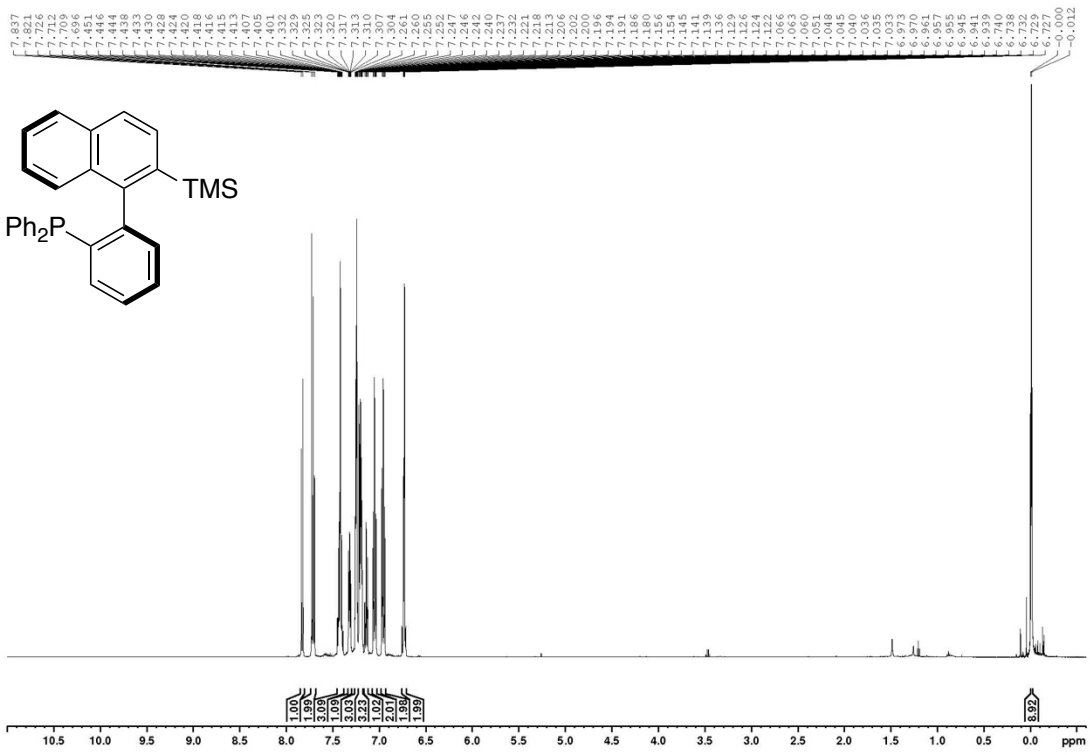

Me
TMS
ppm

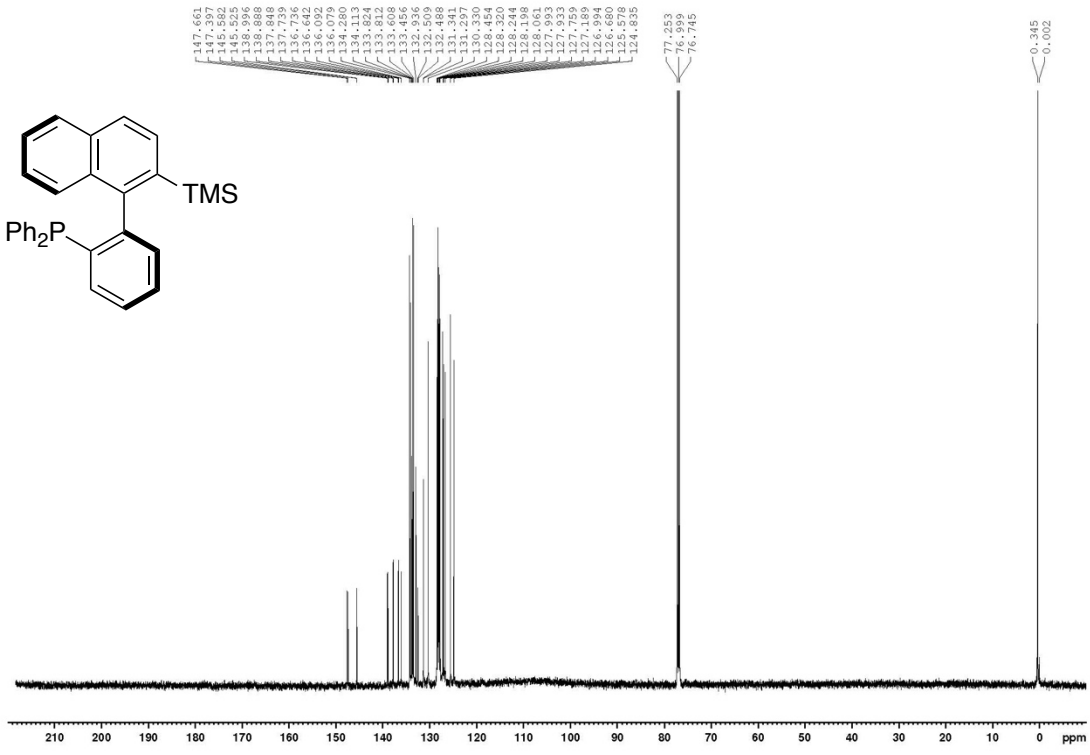

TMS
Cl
7.877
7.876
7.859
7.841
7.840
7.724
7.707
7.517
7.512
7.500
7.499
7.497
7.469
7.467
7.455
7.453
7.450
7.439
7.437
7.410
7.406
7.395
7.391
7.380
7.376
7.373
7.370
7.358
7.355
7.343
7.340
7.337
7.326
7.324
7.300
7.297
7.296
7.286
7.282
7.251
7.249
7.247
7.245
7.234
7.232
7.230
7.228
7.218
1.497
1.429
0.030
-0.000
-0.227
2.03
1.00
0.94
1.10
3.06
1.00
0.97
8.91
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

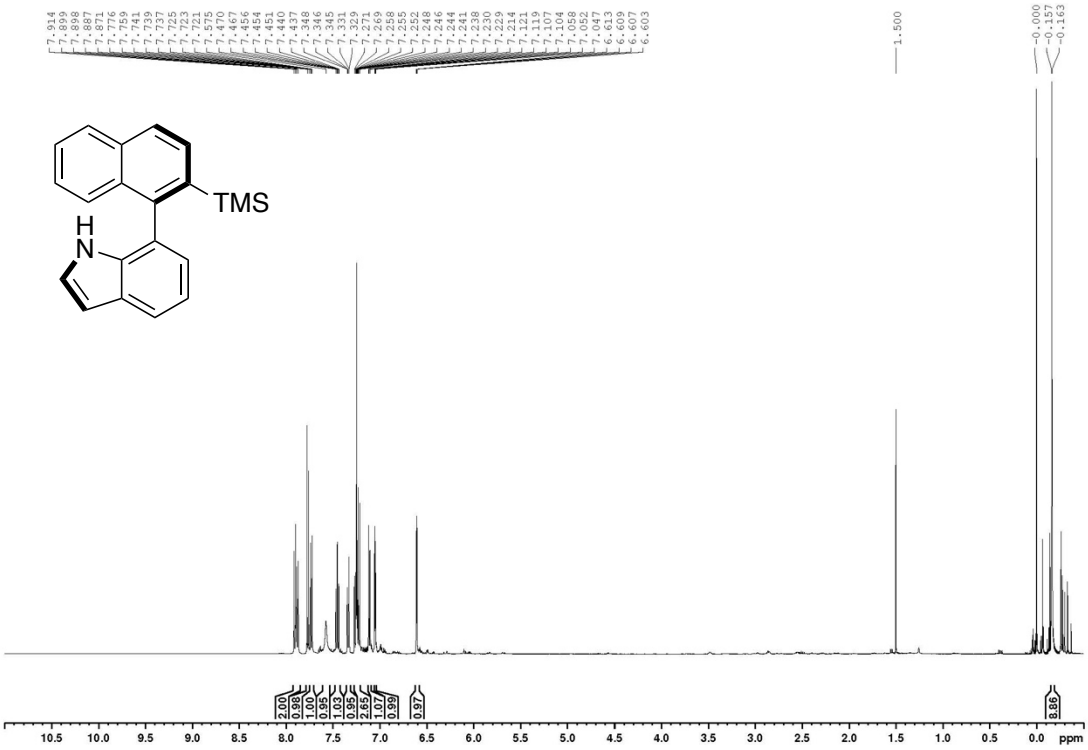

TMS
Cl
143.186
139.665
135.848
134.757
132.952
132.265
131.442
130.077
128.872
128.727
127.441
126.571
125.888
125.738
125.670
125.419
76.811
76.556
76.302
-0.004
-0.473
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

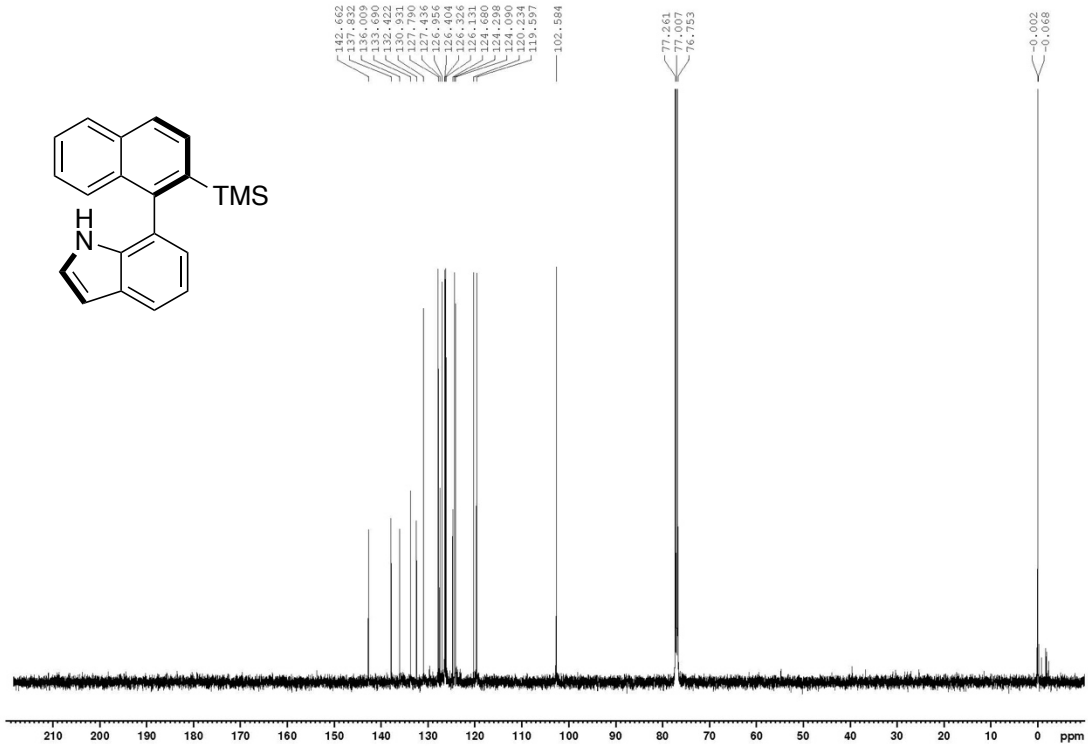

TMS
F
ppm

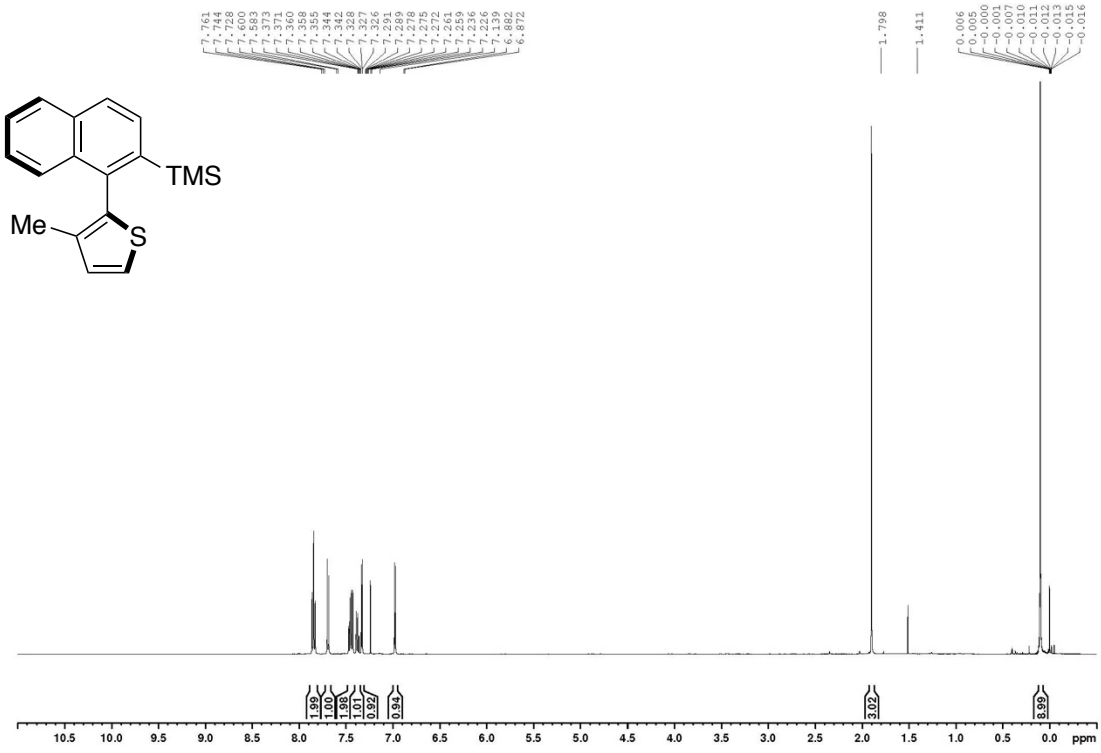

TMS
F
ppm

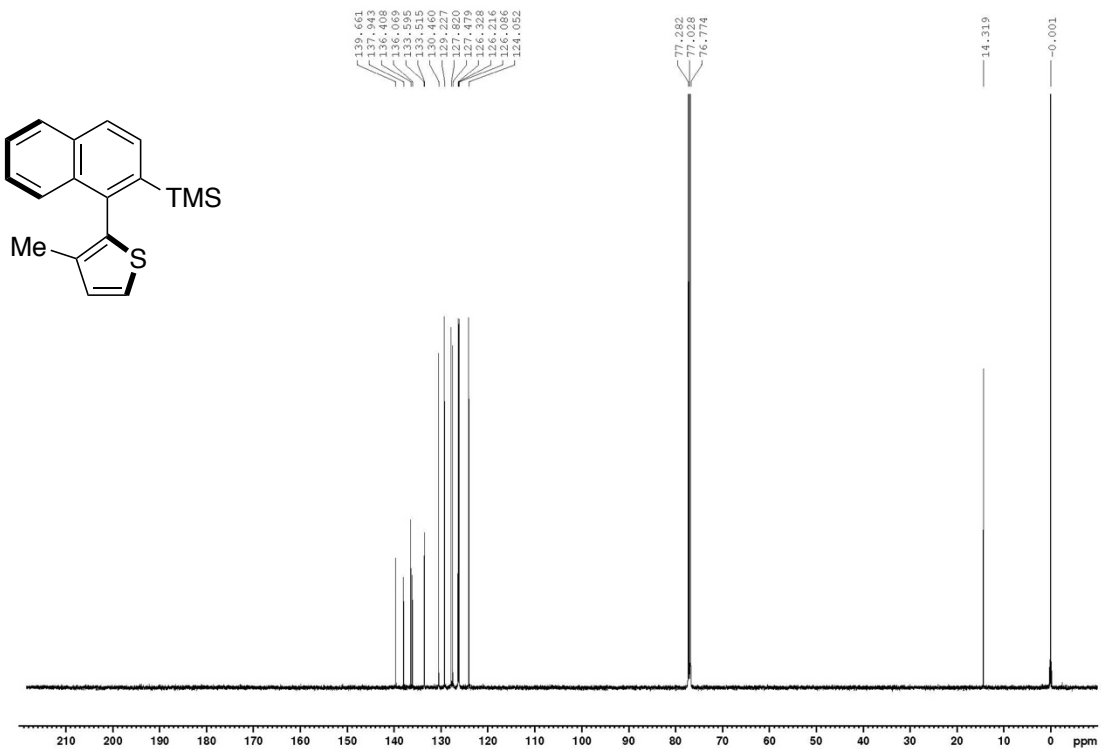

TMS
Ph2P
ppm

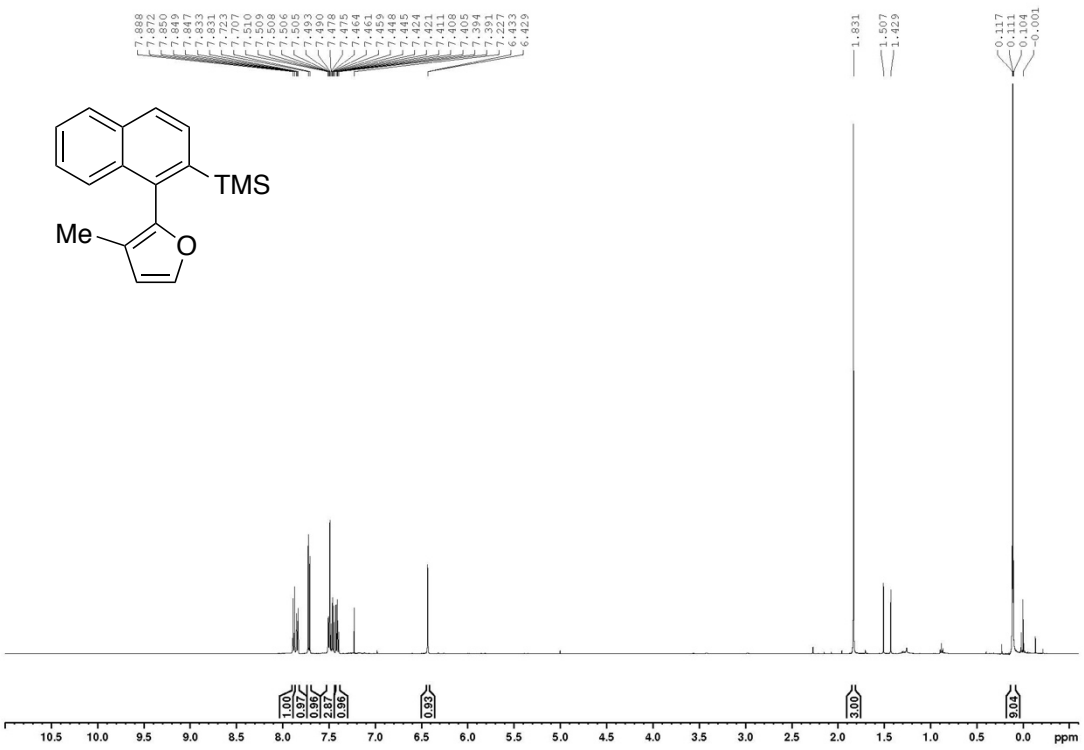

TMS
Ph2P
ppm

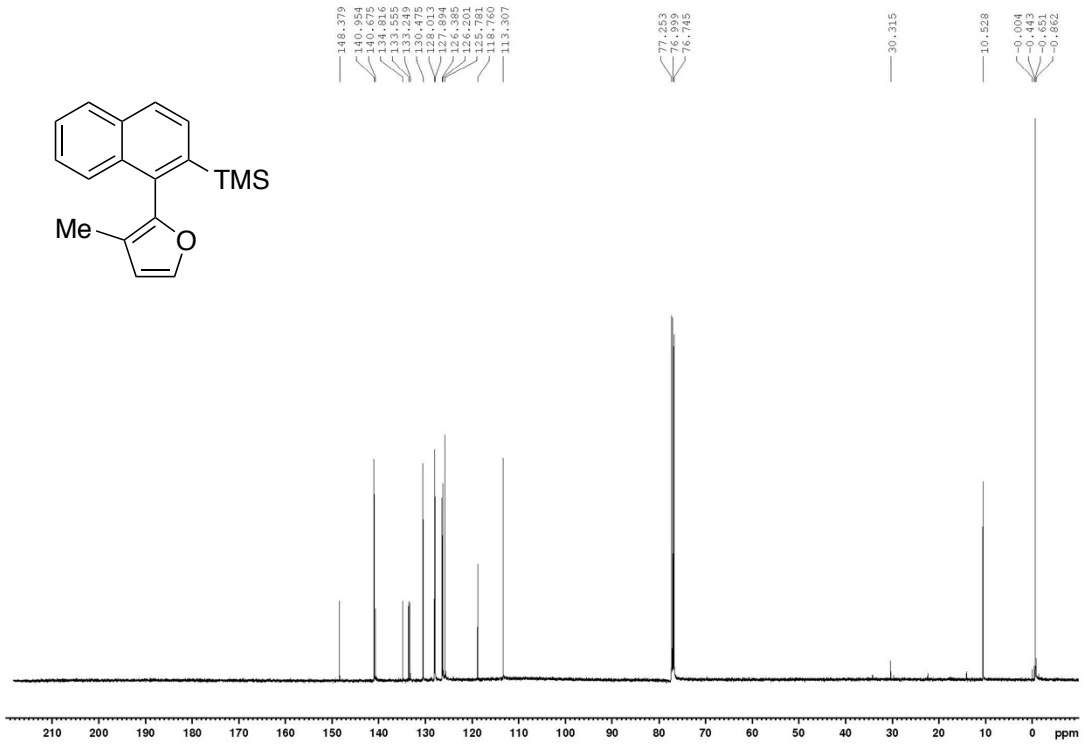

TMS
H
N
ppm

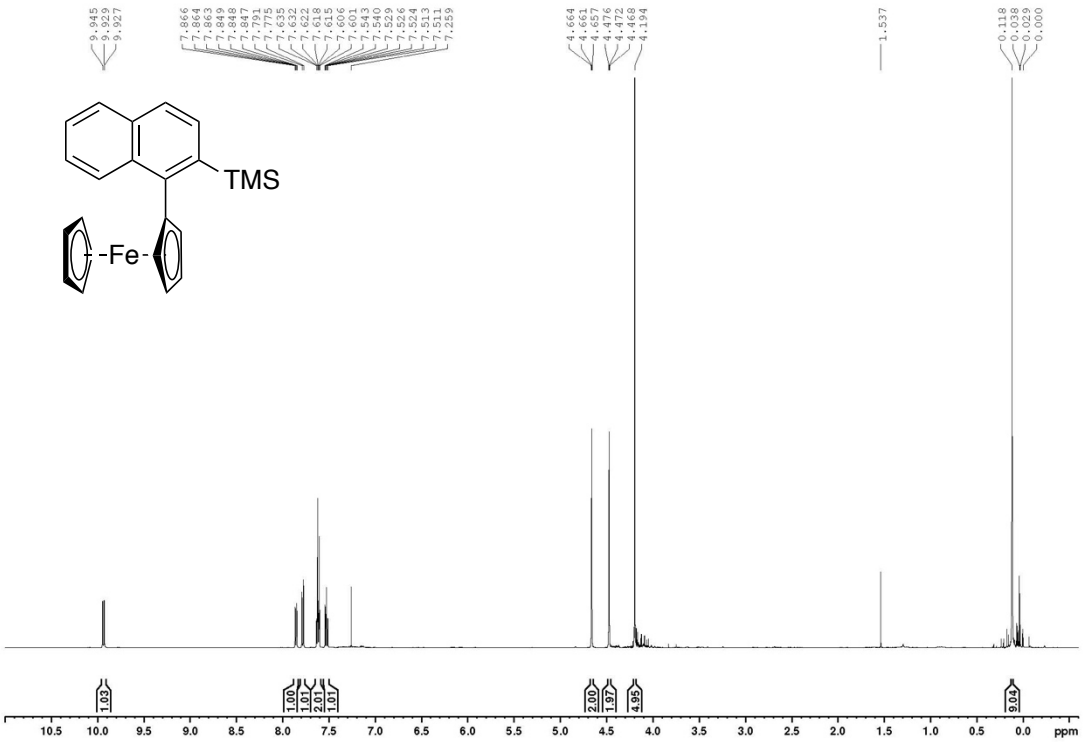

TMS
H
N
ppm

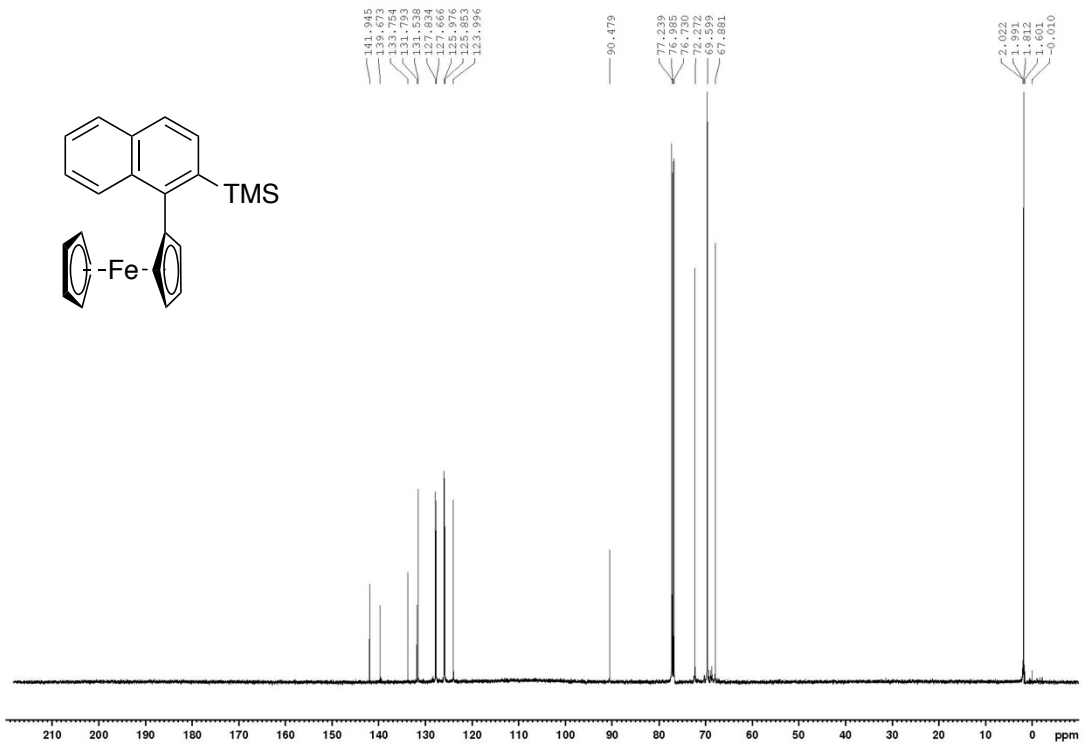

TMS
Me
S
7.761
7.744
7.728
7.600
7.583
7.373
7.371
7.360
7.358
7.355
7.344
7.342
7.328
7.327
7.326
7.291
7.289
7.278
7.275
7.272
7.261
7.259
7.236
7.226
7.139
6.882
6.872
1.798
1.411
0.006
0.005
0.000
-0.001
-0.007
-0.010
-0.011
-0.012
-0.013
-0.015
-0.016
1.99
1.00
1.98
1.01
0.92
0.94
3.02
8.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

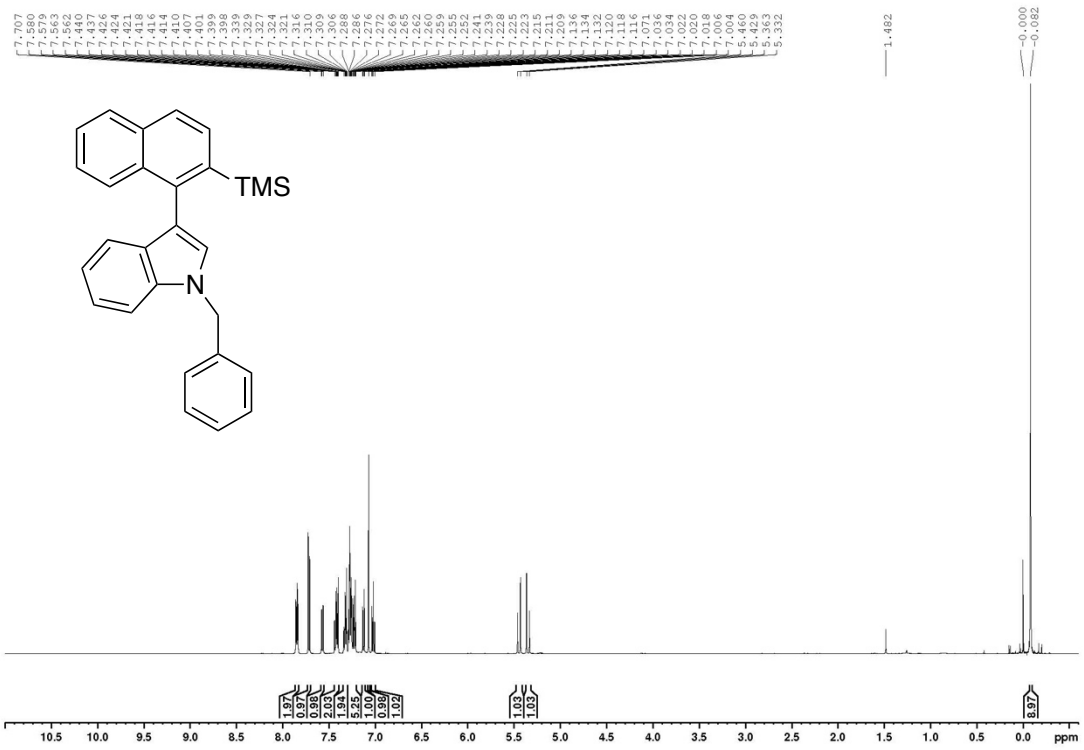

TMS
Me
S
139.661
137.943
136.408
136.069
133.595
133.515
130.460
129.227
127.820
127.479
126.328
126.216
126.086
124.052
77.282
77.028
76.774
14.319
-0.001
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

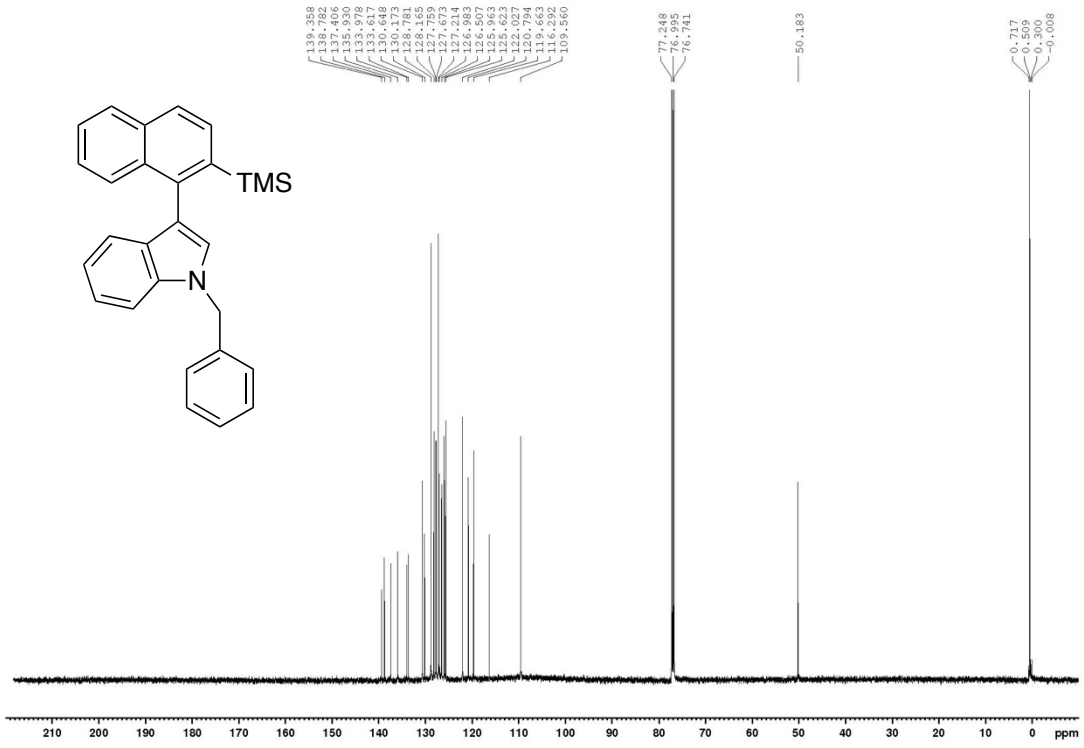

TMS
Me
O
ppm

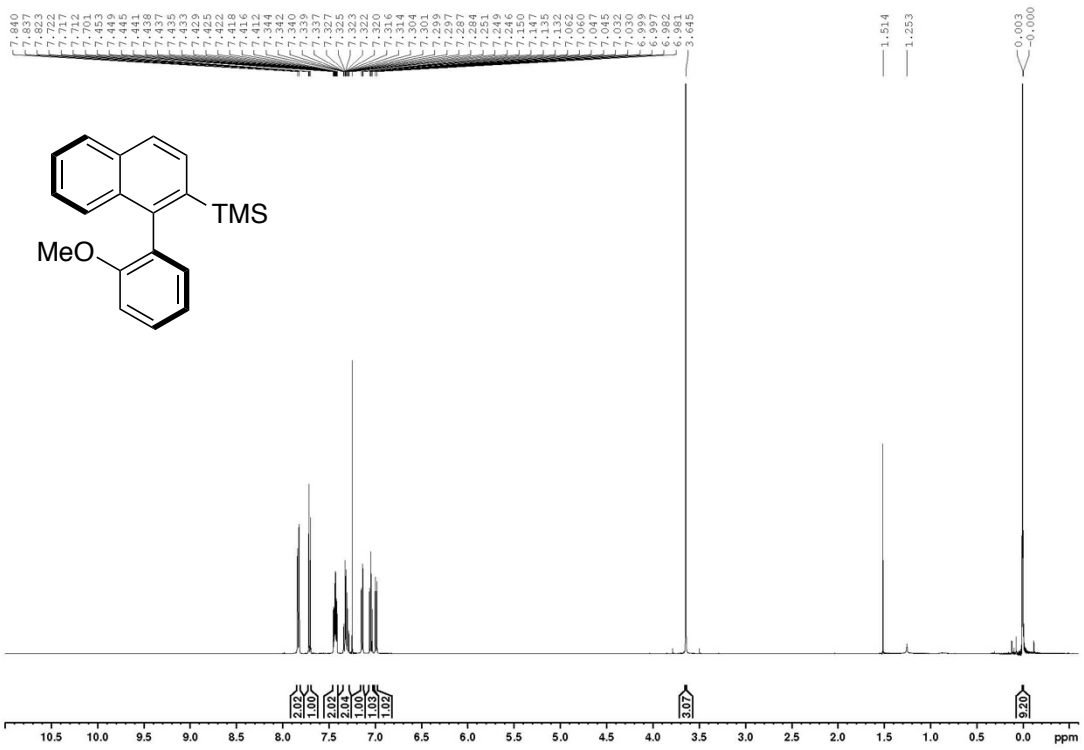

TMS
Me
O
ppm

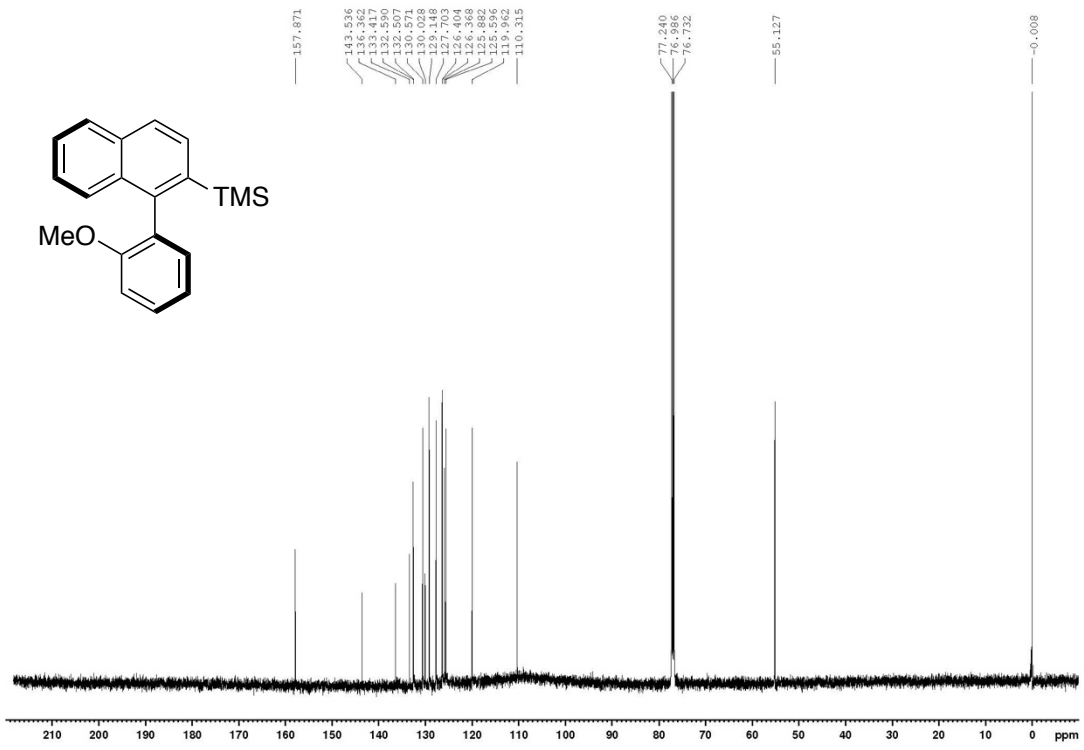

9.945
9.929
9.927
7.866
7.864
7.863
7.849
7.848
7.847
7.791
7.775
7.635
7.632
7.622
7.618
7.615
7.606
7.601
7.543
7.540
7.529
7.526
7.524
7.513
7.511
7.259
4.664
4.661
4.657
4.476
4.472
4.468
4.194
1.537
0.118
0.038
0.029
0.000
TMS
Fe
1.03
1.00
1.01
2.01
1.01
2.00
1.97
4.95
9.04
ppm

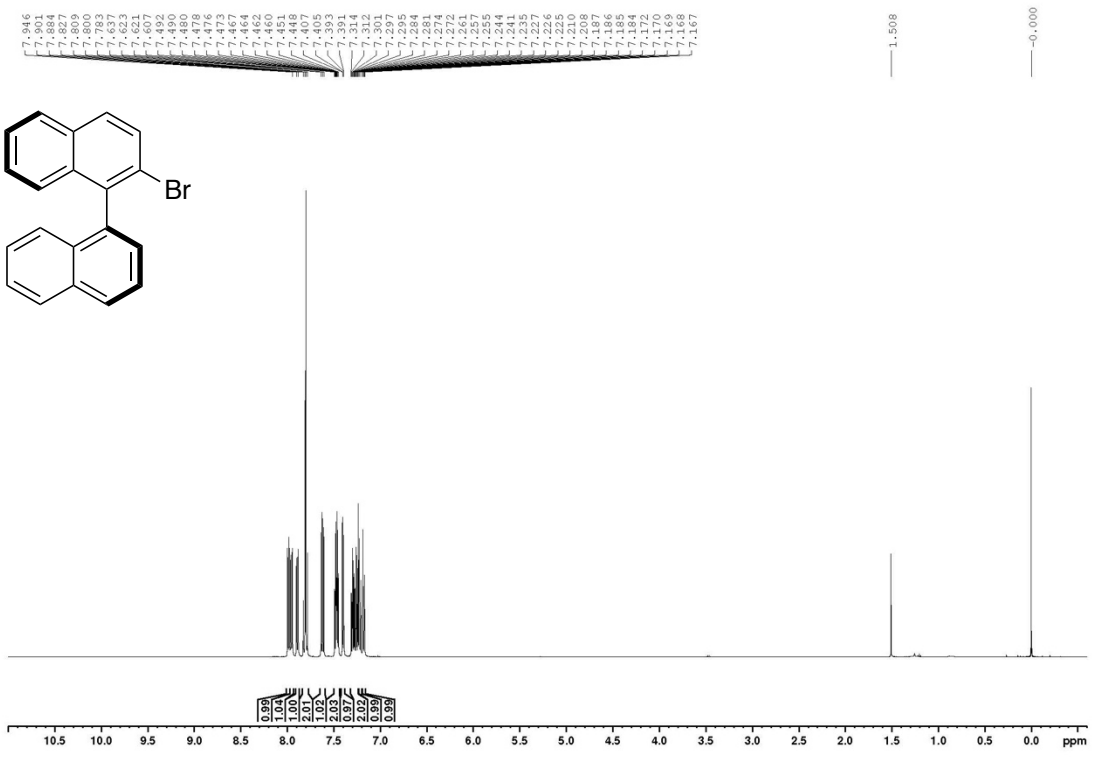

141.945
139.673
133.754
131.793
131.538
127.834
127.666
125.976
125.853
123.996
90.479
77.239
76.835
76.730
72.272
69.599
67.881
2.022
1.991
1.812
1.601
0.010
TMS
Fe
ppm

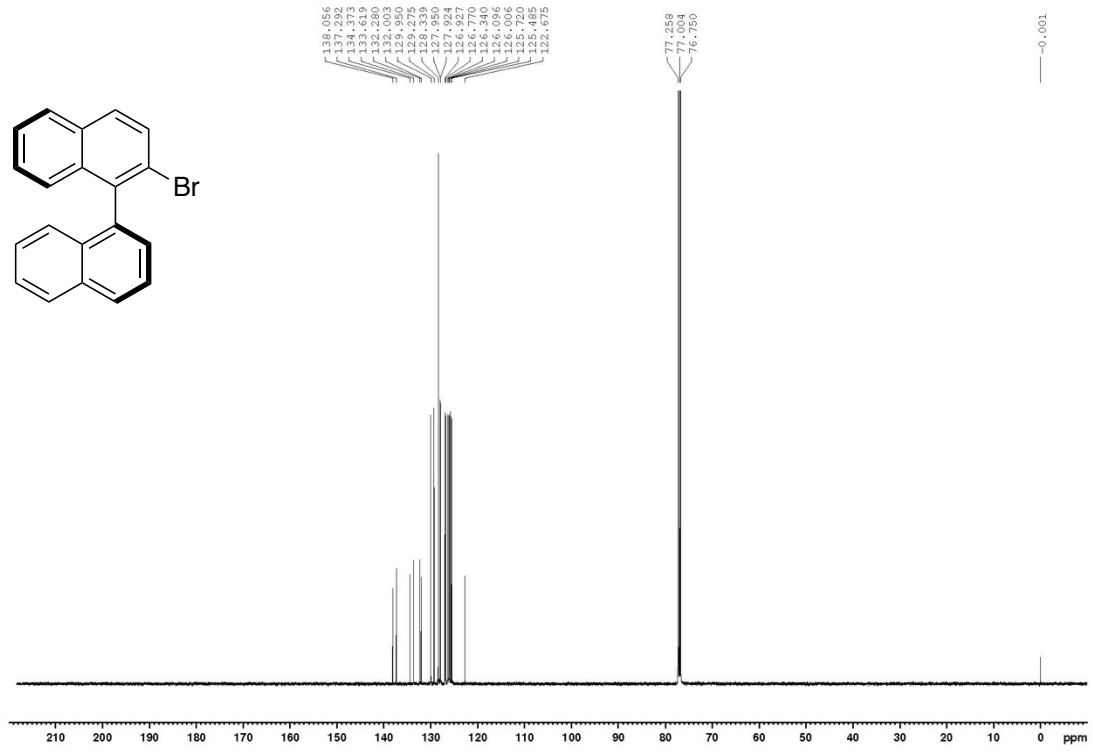

TMS
N
ppm

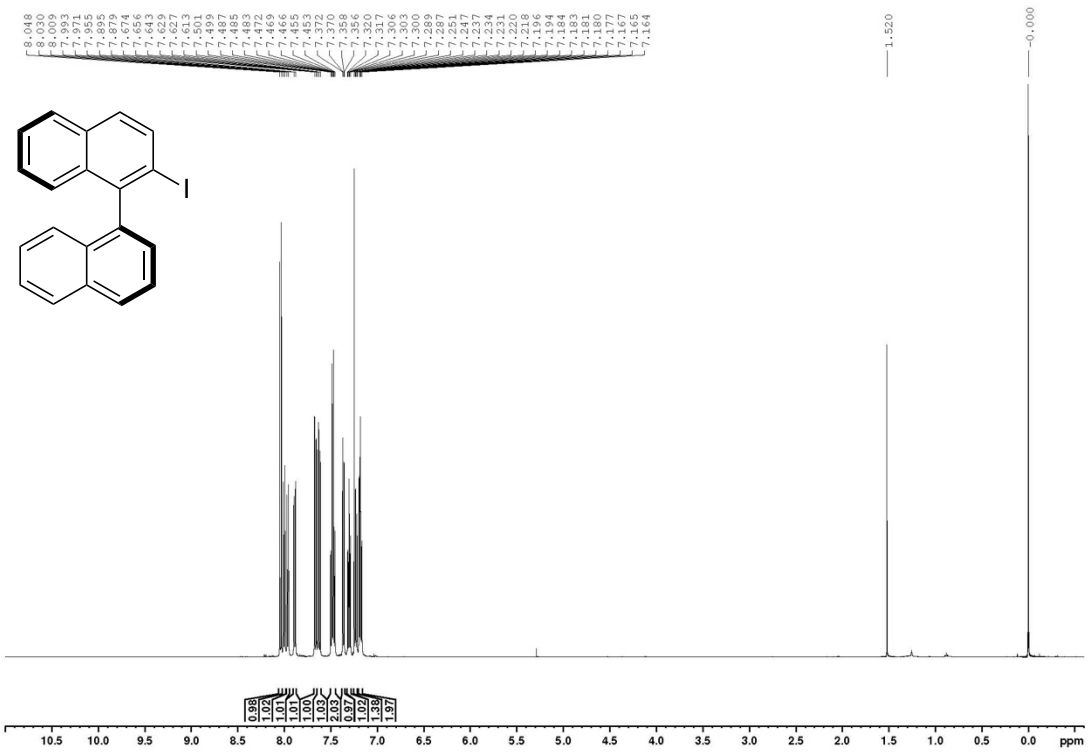

TMS
N
ppm

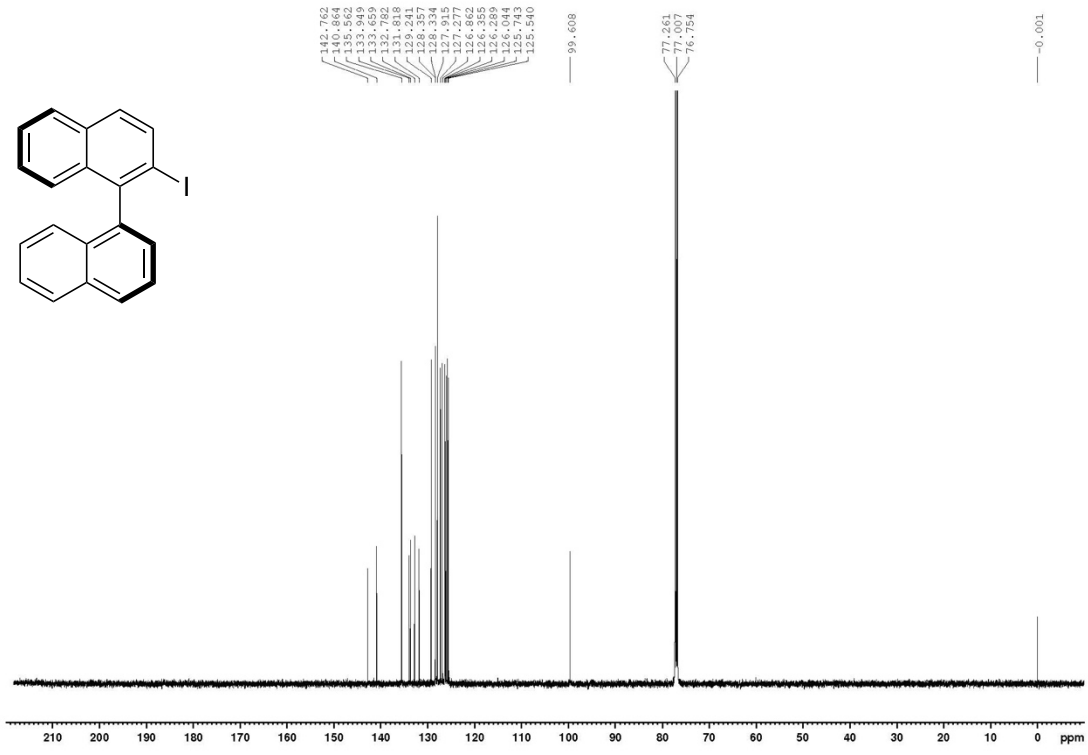

TMS
MeO
ppm

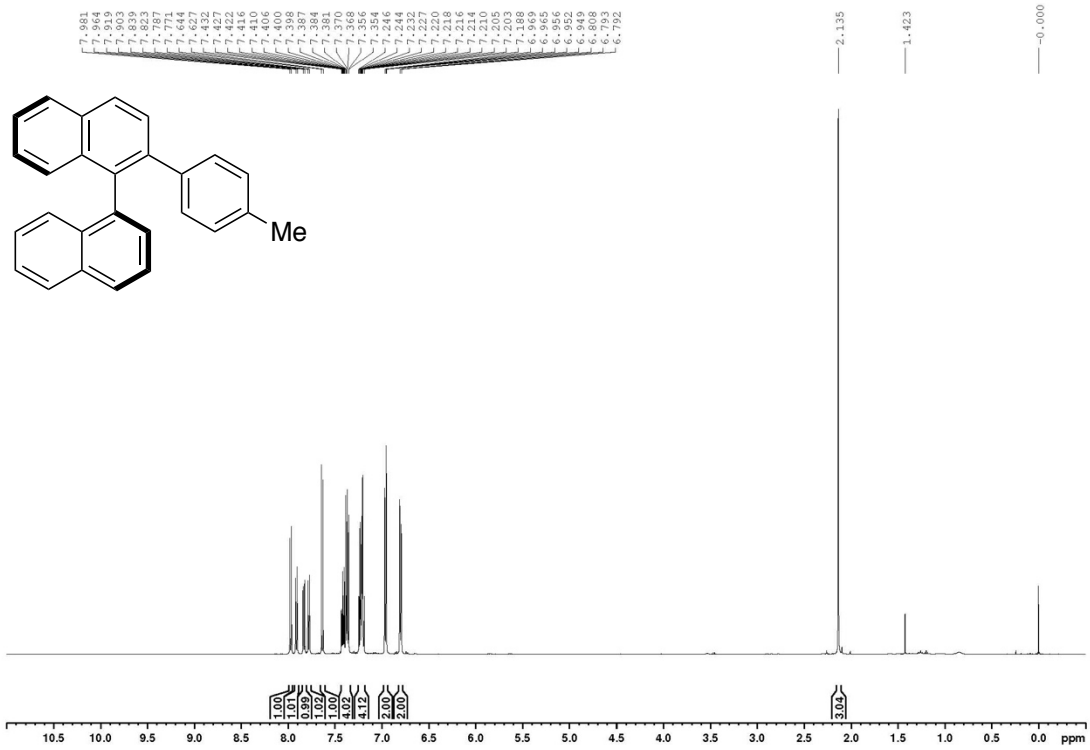

TMS
MeO
ppm

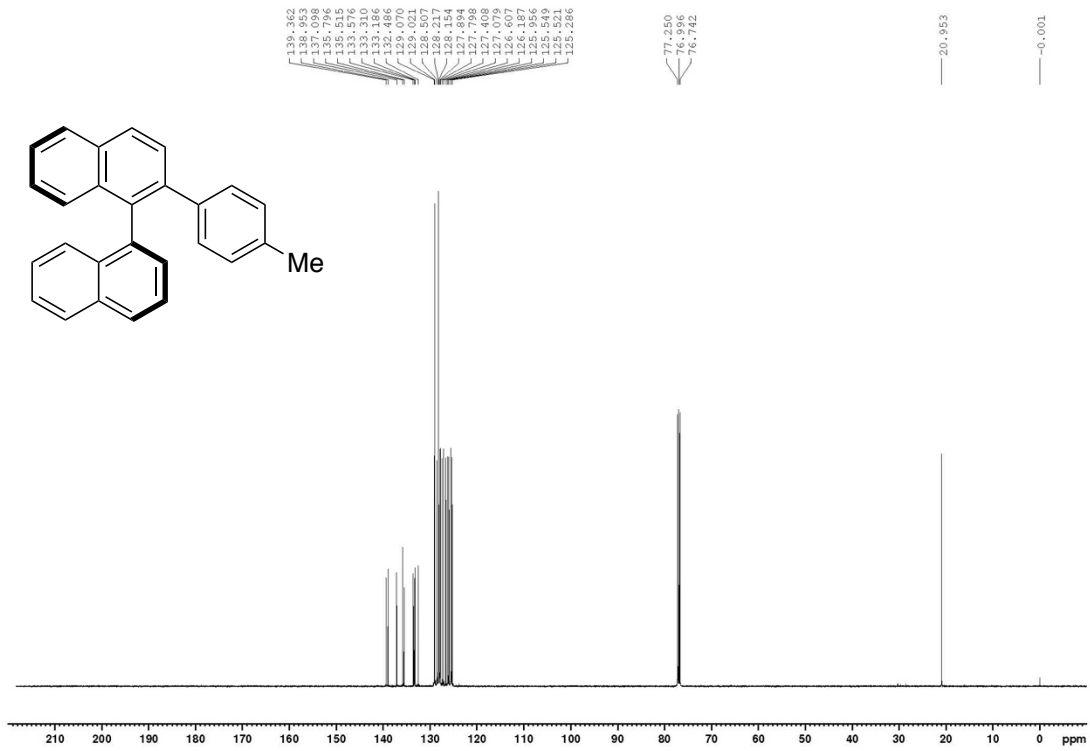

Br
7.946
7.901
7.884
7.827
7.809
7.800
7.783
7.637
7.623
7.621
7.607
7.492
7.490
7.480
7.478
7.476
7.473
7.467
7.464
7.462
7.460
7.451
7.448
7.407
7.405
7.393
7.391
7.314
7.312
7.301
7.297
7.295
7.284
7.281
7.274
7.272
7.261
7.257
7.255
7.244
7.241
7.235
7.227
7.226
7.225
7.210
7.208
7.187
7.186
7.185
7.184
7.172
7.170
7.169
7.168
7.167
1.508
0.000
0.99
1.04
1.00
2.01
1.02
2.03
0.97
2.02
0.99
0.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


Br
138.056
137.292
134.373
133.619
132.280
132.003
129.950
129.375
128.339
127.950
127.924
126.927
126.770
126.340
126.096
126.096
125.720
125.485
122.675
77.258
77.004
76.750
0.001
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.048
8.030
8.009
7.993
7.971
7.955
7.895
7.879
7.674
7.656
7.643
7.629
7.627
7.613
7.601
7.499
7.487
7.485
7.483
7.472
7.469
7.466
7.455
7.453
7.372
7.370
7.358
7.356
7.320
7.317
7.306
7.303
7.300
7.289
7.287
7.251
7.247
7.237
7.234
7.231
7.220
7.218
7.196
7.194
7.184
7.183
7.181
7.180
7.177
7.167
7.165
7.164
1.520
0.000
0.98
1.04
1.01
1.01
1.00
1.03
2.03
0.97
1.02
1.38
1.97
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

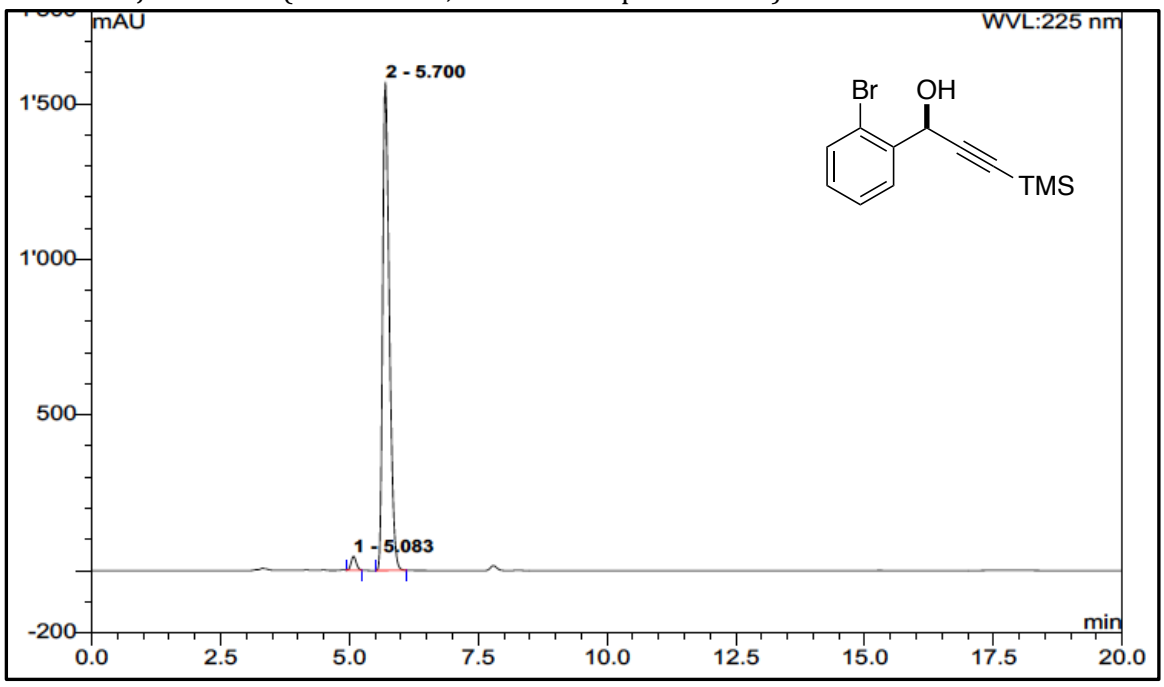

142.762
140.864
135.562
133.949
133.659
132.782
131.818
129.241
128.357
128.334
127.915
127.277
126.862
126.355
126.289
126.044
125.743
125.540
99.608
77.261
77.007
76.754
0.001
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.981
7.964
7.919
7.903
7.839
7.823
7.787
7.771
7.644
7.627
7.432
7.427
7.422
7.416
7.410
7.406
7.400
7.398
7.387
7.384
7.381
7.370
7.368
7.356
7.354
7.246
7.244
7.232
7.227
7.220
7.218
7.216
7.214
7.210
7.205
7.203
7.188
6.969
6.965
6.956
6.952
6.949
6.908
6.903
6.792
2.135
1.423
0.000
Me
1.00
1.01
0.99
1.02
1.00
4.02
4.12
2.00
2.00
3.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

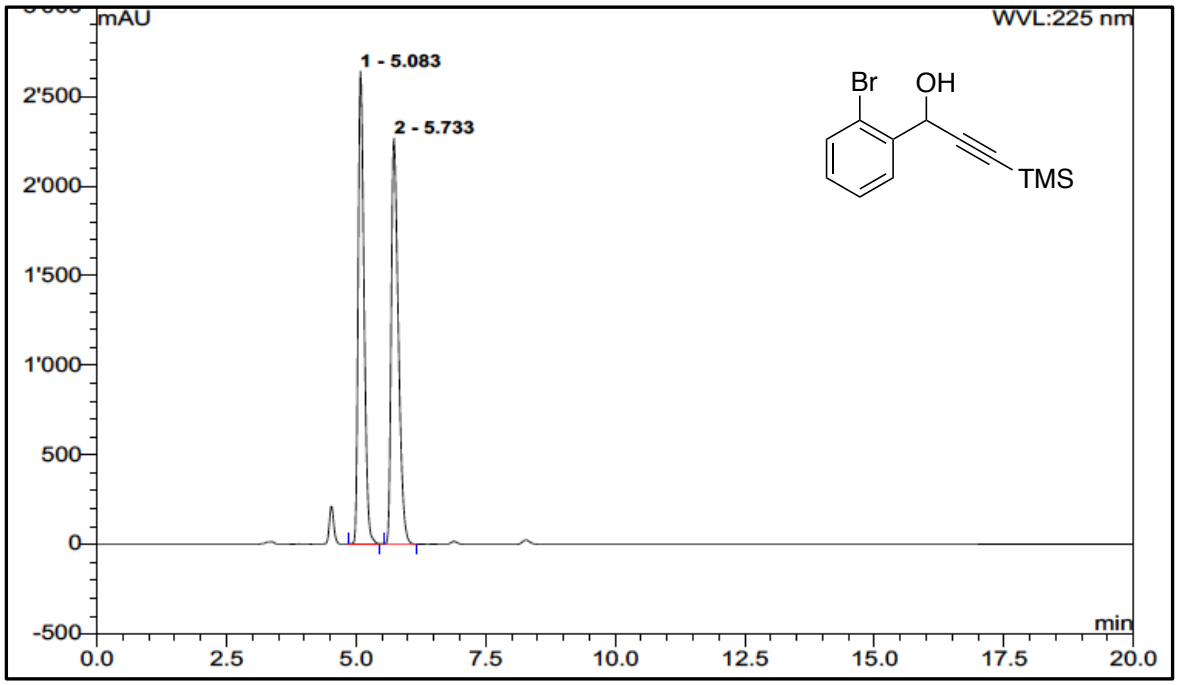

139.362
138.953
137.098
135.796
135.515
133.575
133.310
133.186
132.486
129.070
129.021
128.807
128.217
128.154
127.894
127.798
127.408
127.079
126.607
126.187
125.956
125.549
125.521
125.286
77.250
76.996
76.742
20.953
0.001
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

HPLC Data

Chiralcel OJ-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 90:10)

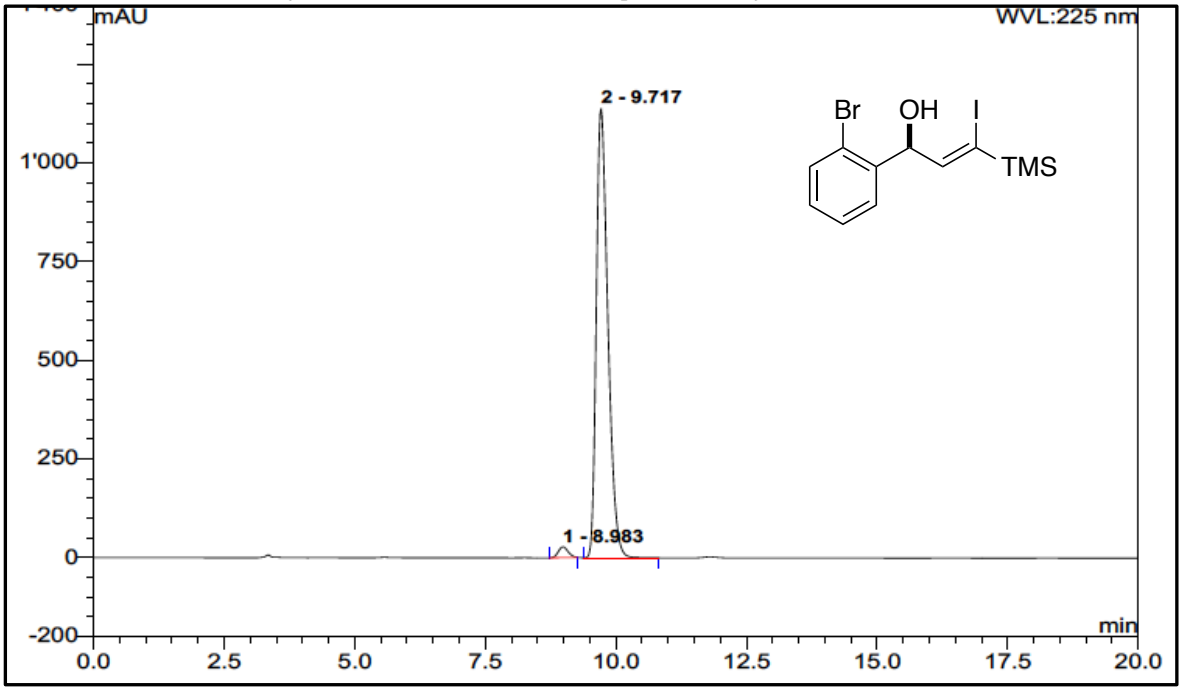


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5.08	n.a.		44.619	5.103	2.12	n.a.	BMB*
2	5.70	n.a.		1568.925	235.903	97.88	n.a.	BMB*
Total:				1613.544	241.006	100.00	0.000	

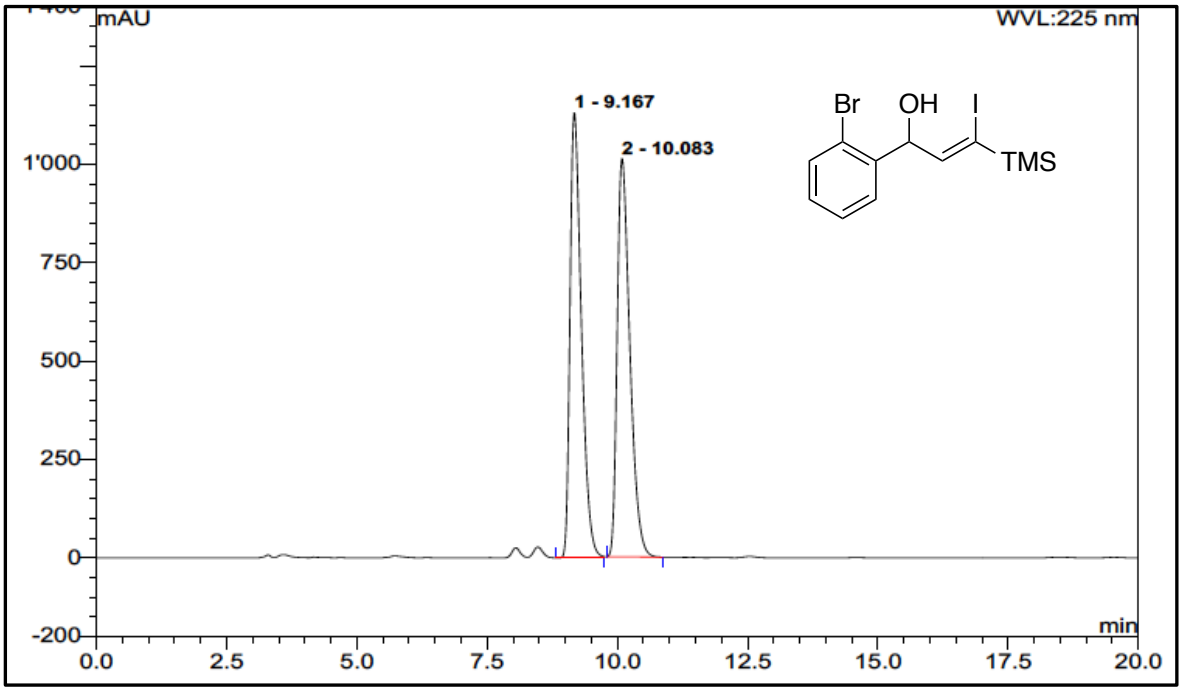


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5.08	n.a.		2637.572	345.114	48.90	n.a.	BMB*
2	5.73	n.a.		2264.099	360.656	51.10	n.a.	BMB*
Total:				4901.671	705.770	100.00	0.000	

Chiralcel OJ-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 98:2)

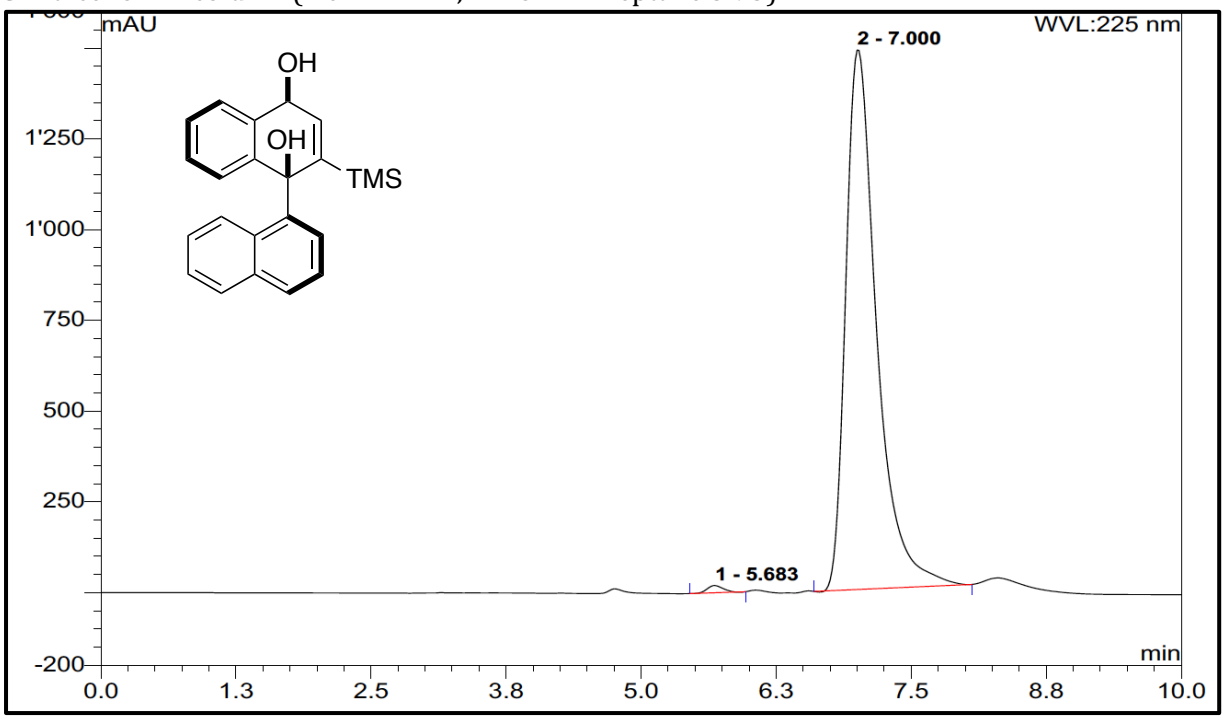


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	8.98	n.a.		27.349	5.937	1.99	n.a.	BMB*
2	9.72	n.a.		1138.126	292.377	98.01	n.a.	BMB*
Total:				1165.475	298.315	100.00	0.000	



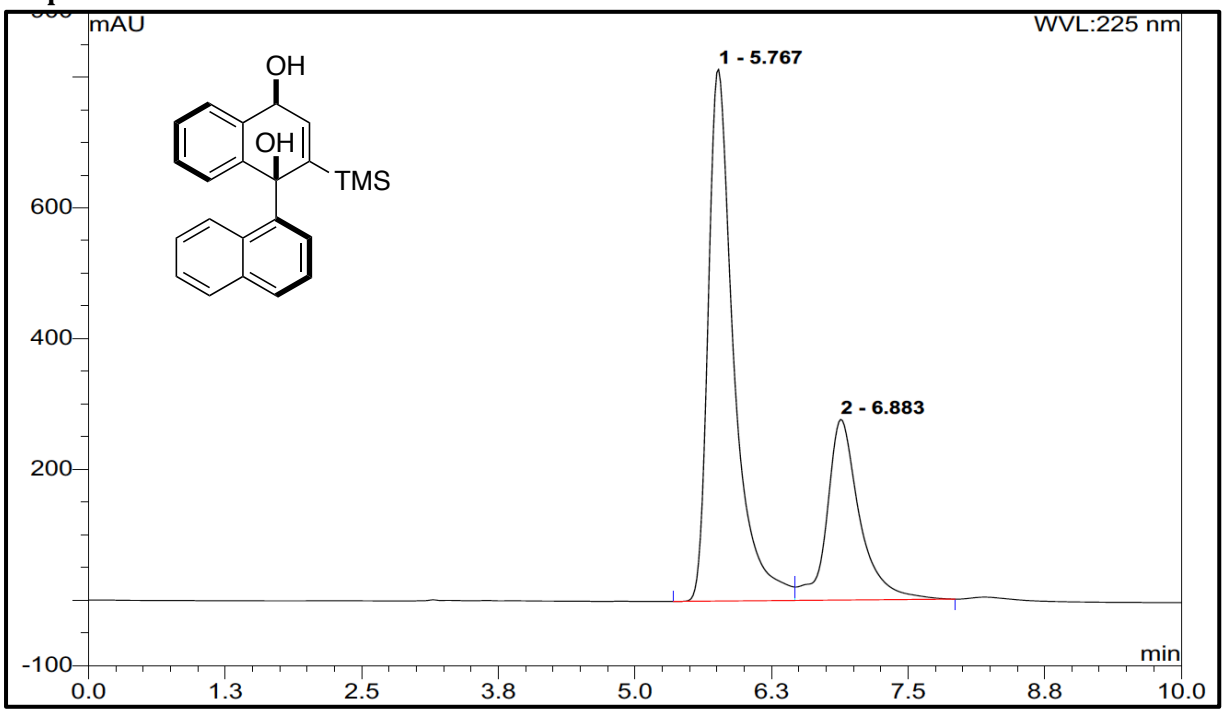
No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	9.17	n.a.		1130.869	286.009	50.05	n.a.	BM *
2	10.08	n.a.		1011.843	285.441	49.95	n.a.	BMB*
Total:				2142.712	571.450	100.00	0.000	

Chiralcel OD-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 5:95)



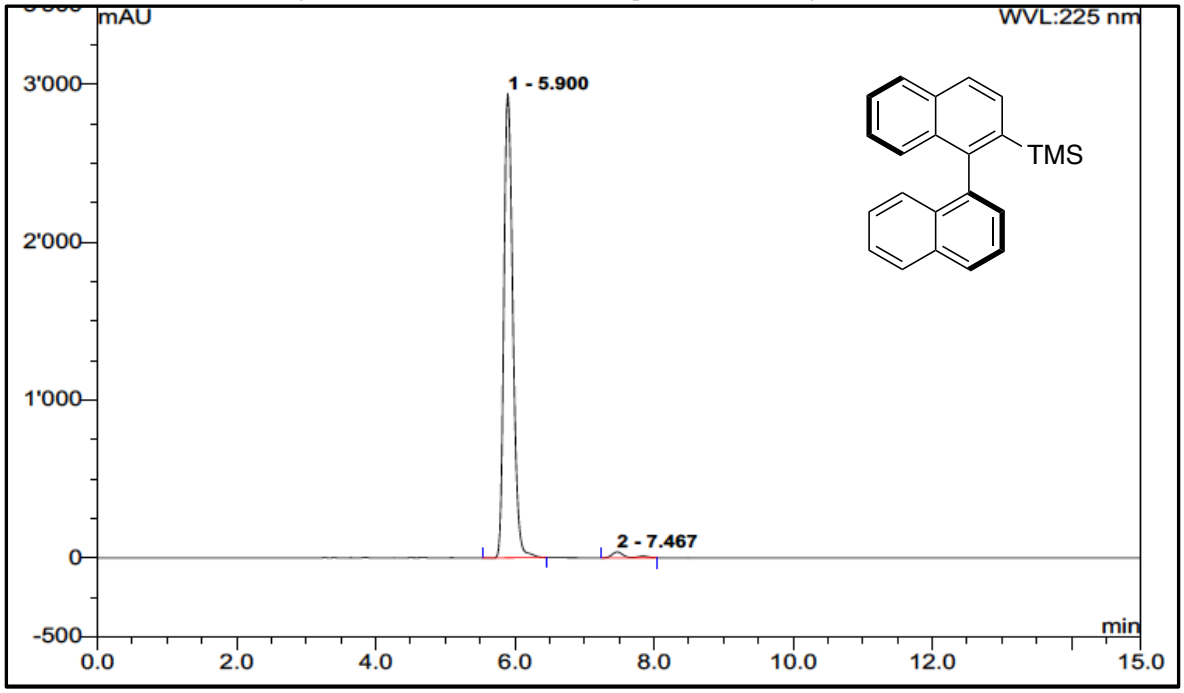
No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5,68	n.a.		19,985	3,311	0,67	n.a.	BMB*
2	7,00	n.a.		1486,178	493,179	99,33	n.a.	BMB*
Total:				1506,164	496,490	100,00	0,000	

Prepared from Precursor with e.r. 70:30

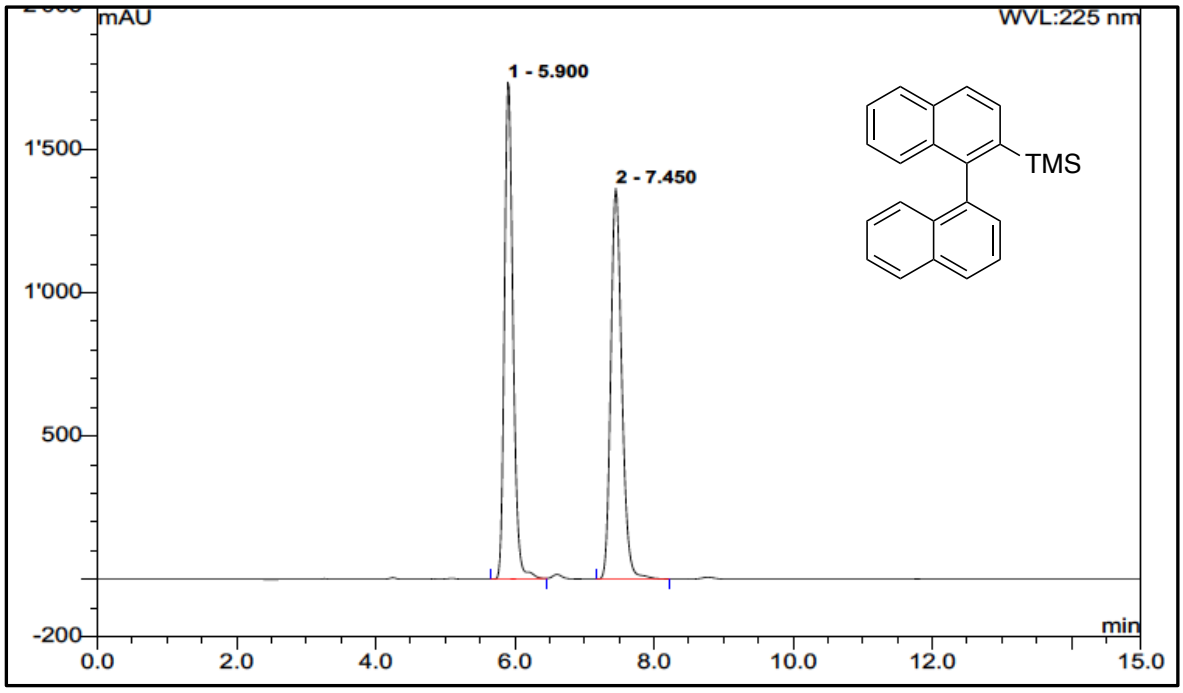


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5,77	n.a.		813,648	221,575	69,89	n.a.	BM *
2	6,88	n.a.		276,374	95,458	30,11	n.a.	MB*
Total:				1090,022	317,033	100,00	0,000	

Chiralcel OD-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

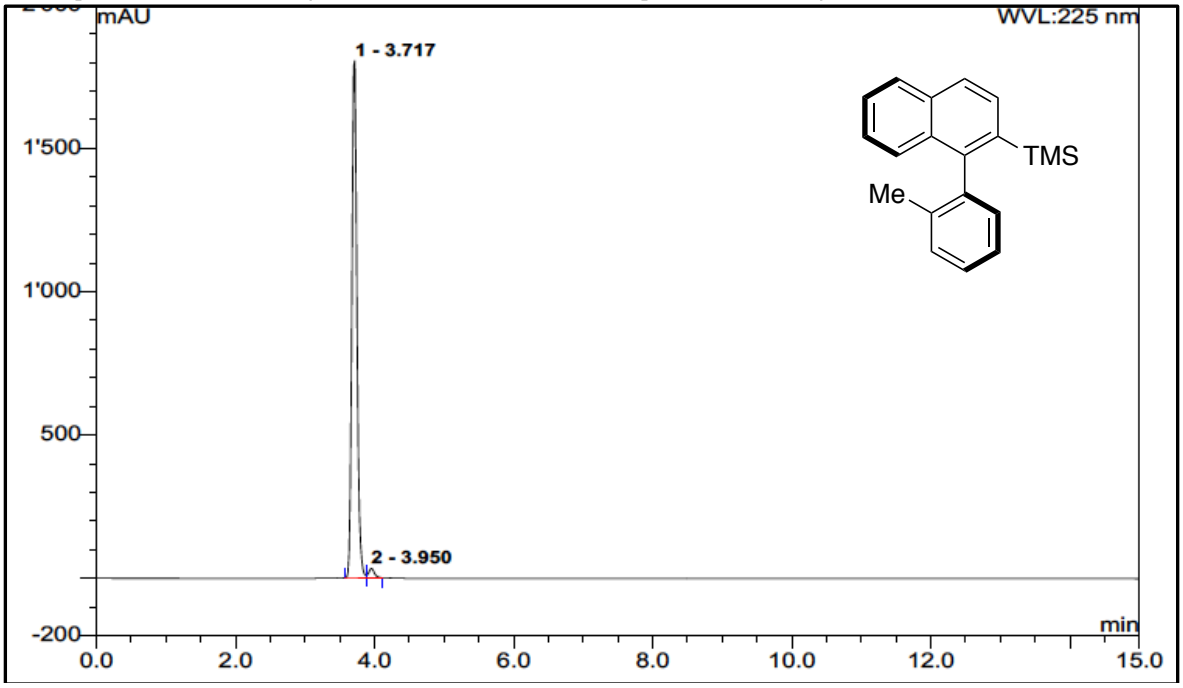


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5.90	n.a.		2940.475	439.621	98.06	n.a.	BMB*
2	7.47	n.a.		37.885	8.694	1.94	n.a.	BMB*
Total:				2978.360	448.315	100.00	0.000	

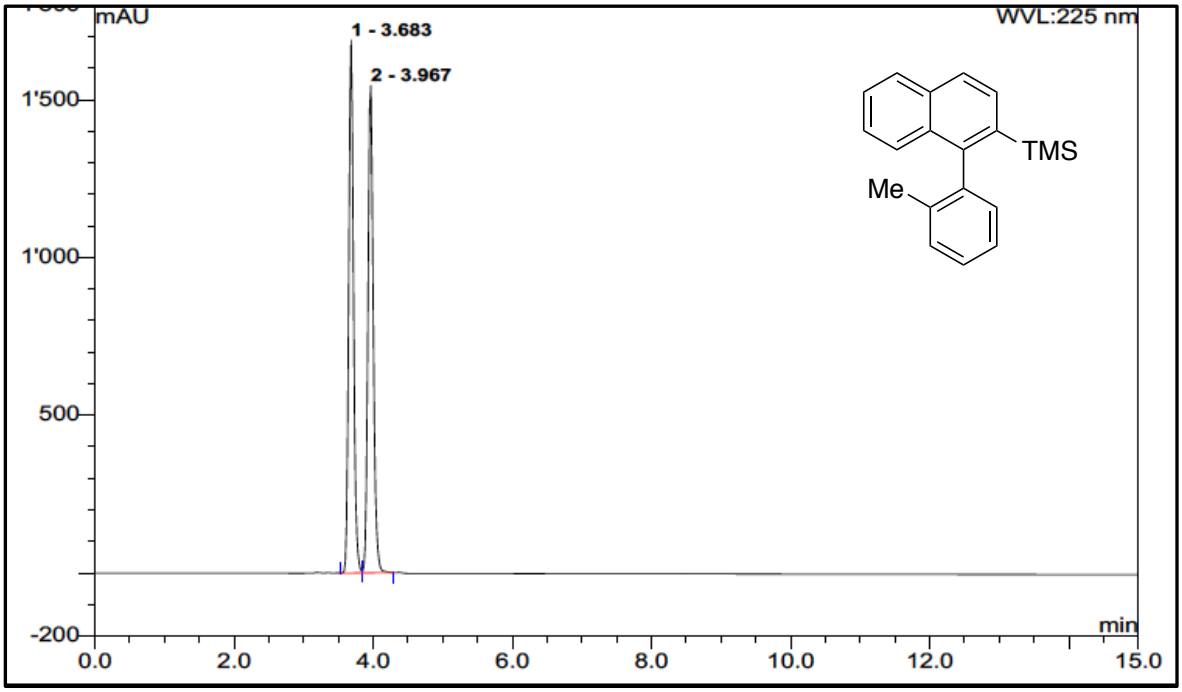


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5.90	n.a.		1732.948	248.395	49.81	n.a.	BMB*
2	7.45	n.a.		1362.589	250.315	50.19	n.a.	BMB*
Total:				3095.537	498.709	100.00	0.000	

Chiralpak AD-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

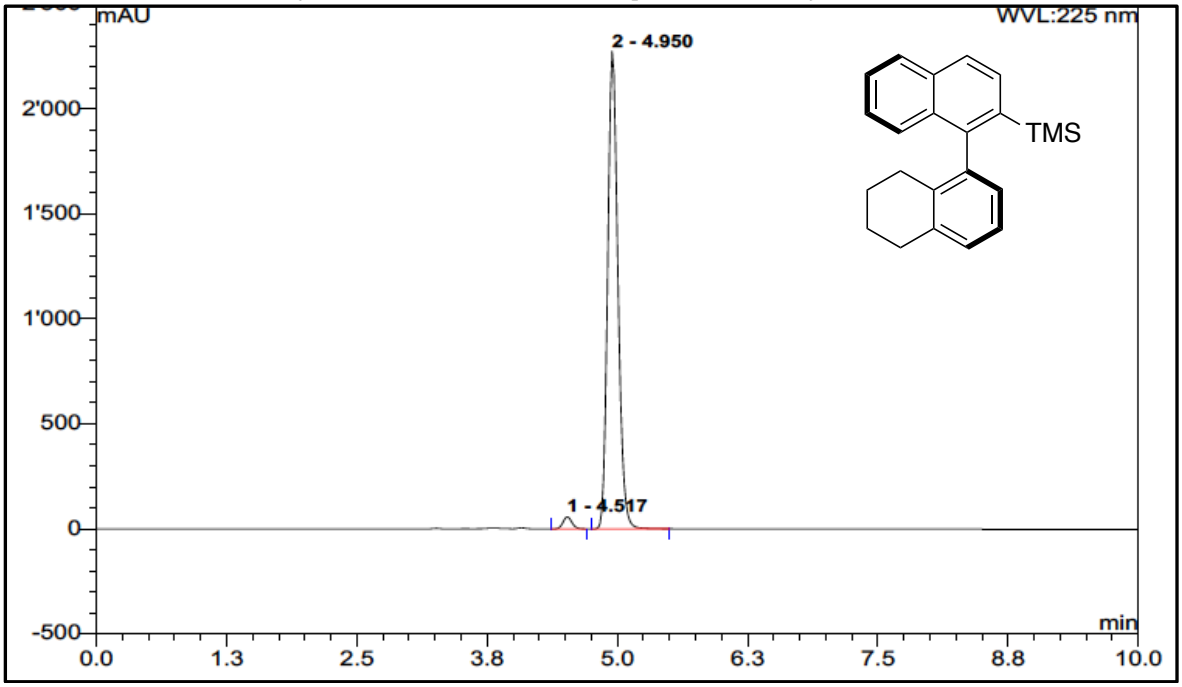


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	3.72	n.a.		1805.081	152.480	97.90	n.a.	BM *
2	3.95	n.a.		33.472	3.275	2.10	n.a.	MB*
Total:				1838.553	155.755	100.00	0.000	

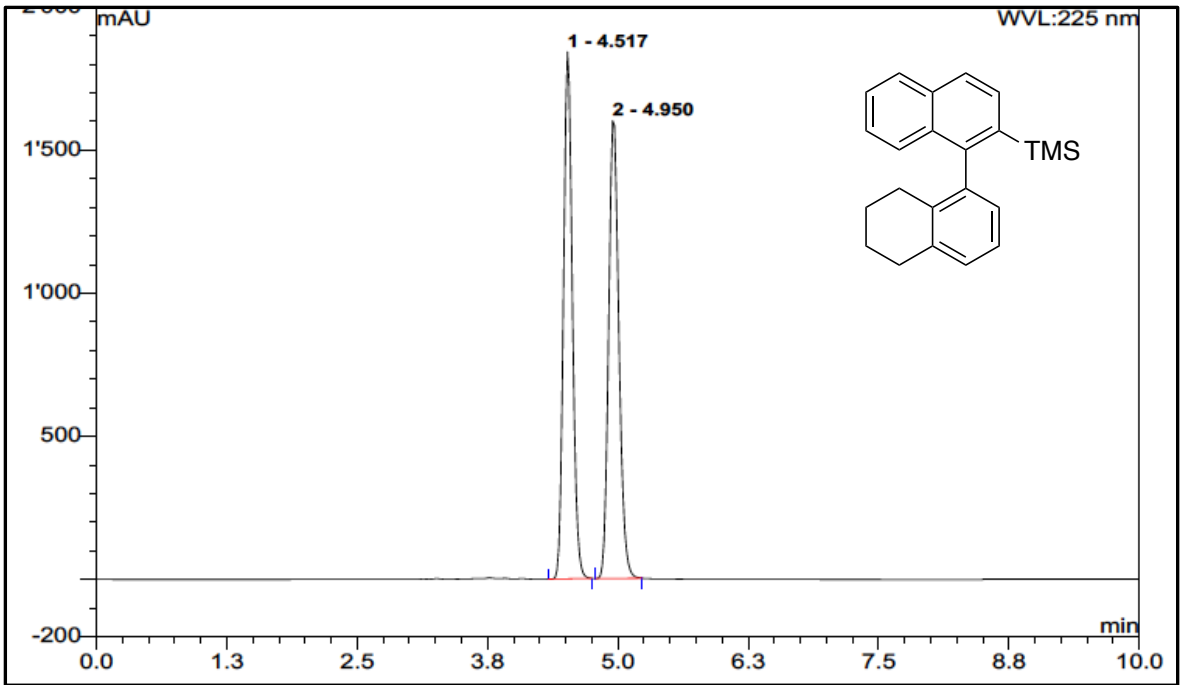


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	3.68	n.a.		1688.134	134.264	49.44	n.a.	BM *
2	3.97	n.a.		1544.370	137.332	50.56	n.a.	MB*
Total:				3232.504	271.596	100.00	0.000	

Chiralcel OD-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

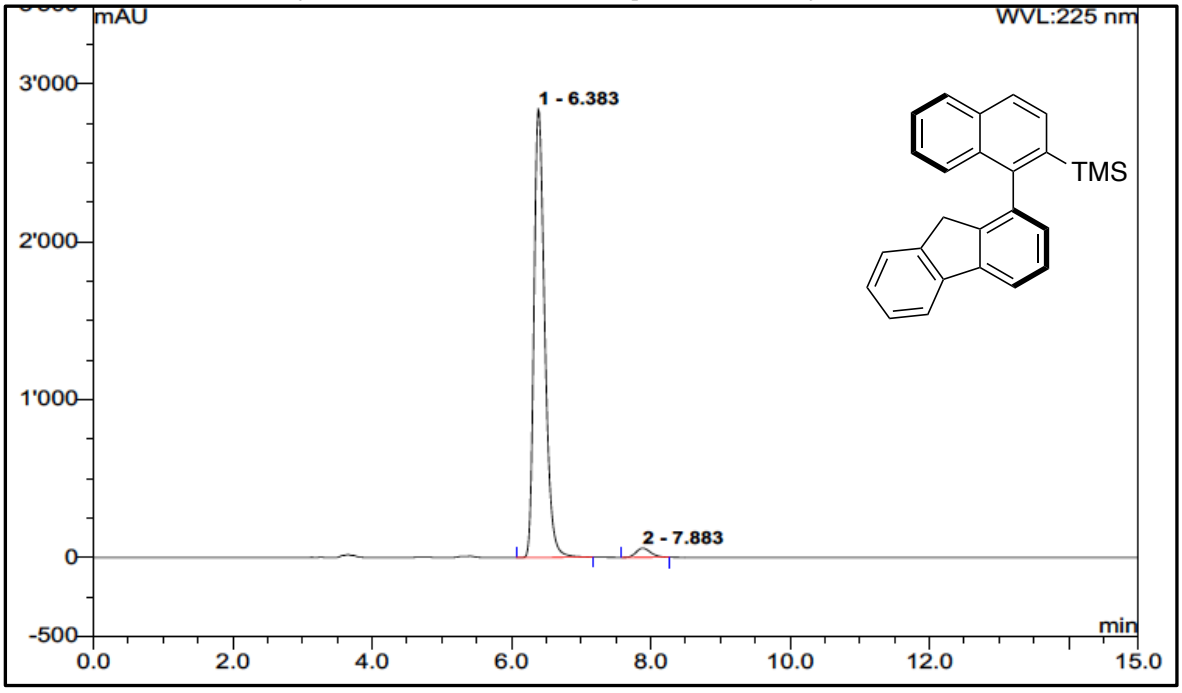


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	4.52	n.a.		57.842	5.645	2.13	n.a.	BMB*
2	4.95	n.a.		2274.343	258.776	97.87	n.a.	BMB*
Total:				2332.185	264.421	100.00	0.000	

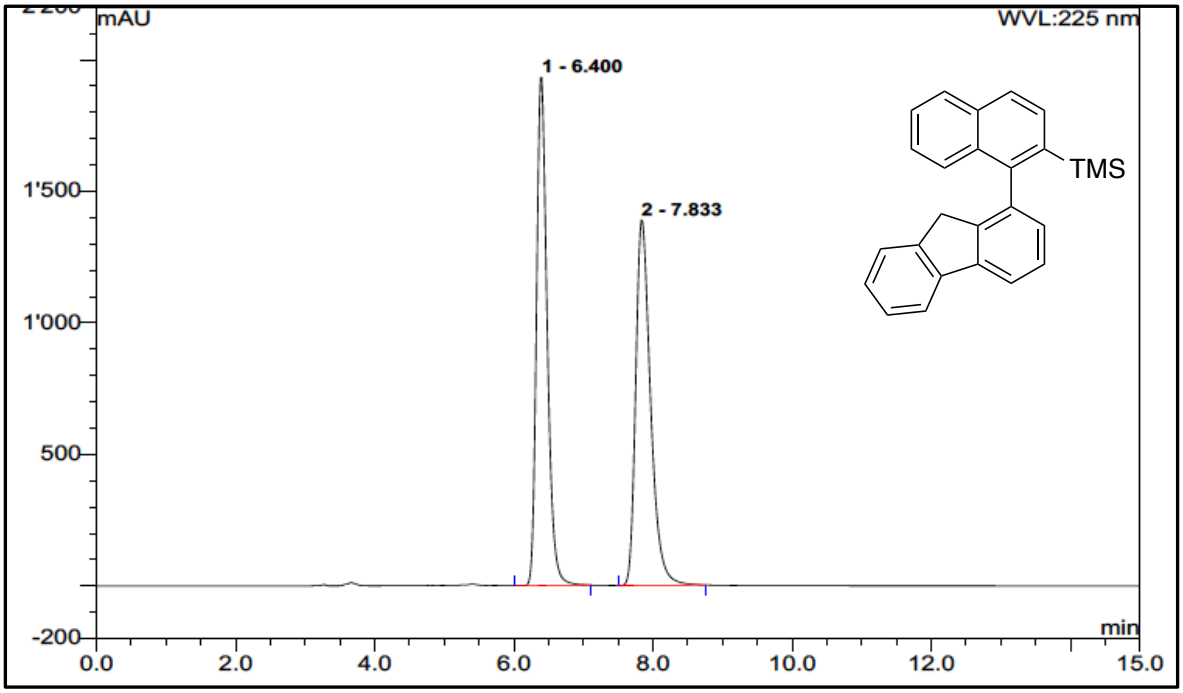


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	4.52	n.a.		1840.613	181.160	49.80	n.a.	BMB*
2	4.95	n.a.		1598.725	182.623	50.20	n.a.	BMB*
Total:				3439.338	363.783	100.00	0.000	

Chiralcel OD-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

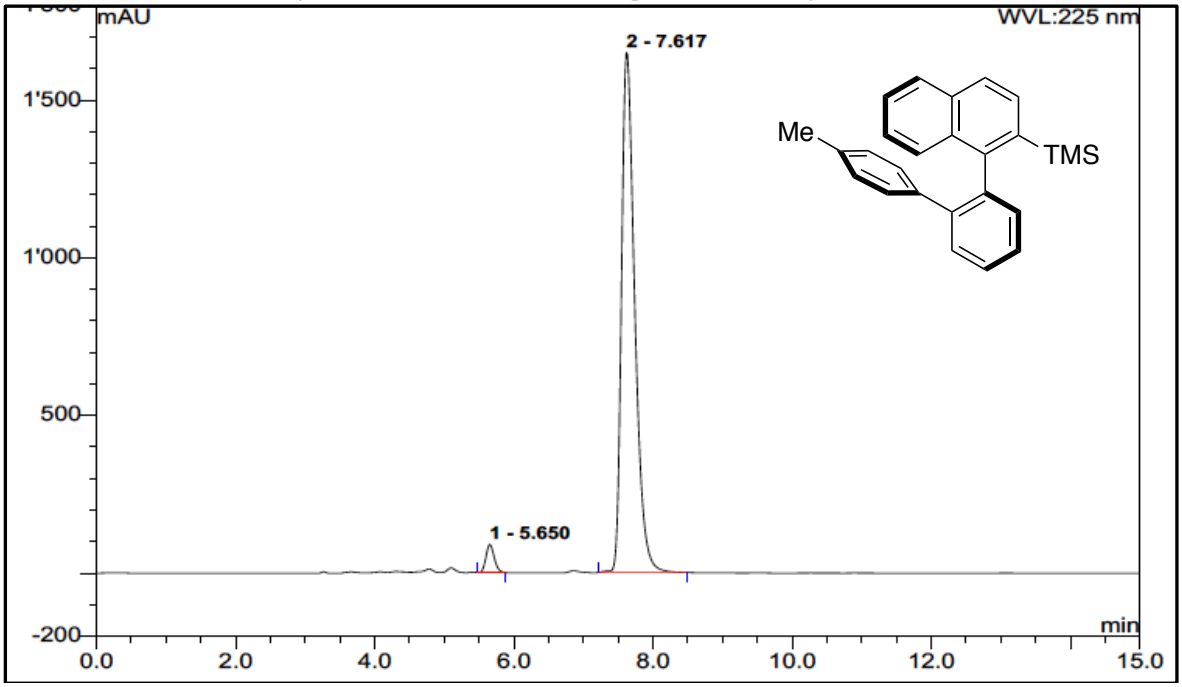


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	6.38	n.a.		2842.952	508.757	97.30	n.a.	BMB*
2	7.88	n.a.		58.667	14.139	2.70	n.a.	BMB*
Total:				2901.619	522.896	100.00	0.000	

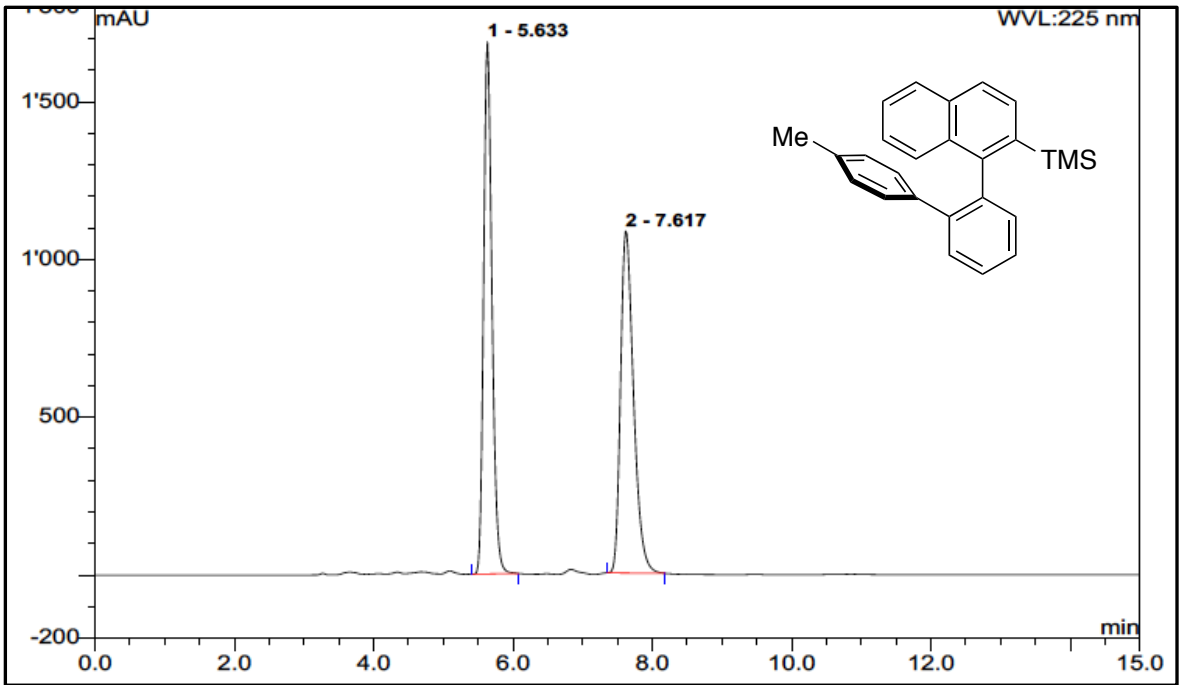


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	6.40	n.a.		1930.490	341.611	49.92	n.a.	BMB*
2	7.83	n.a.		1388.806	342.711	50.08	n.a.	BMB*
Total:				3319.296	684.322	100.00	0.000	

Chiralcel OD-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

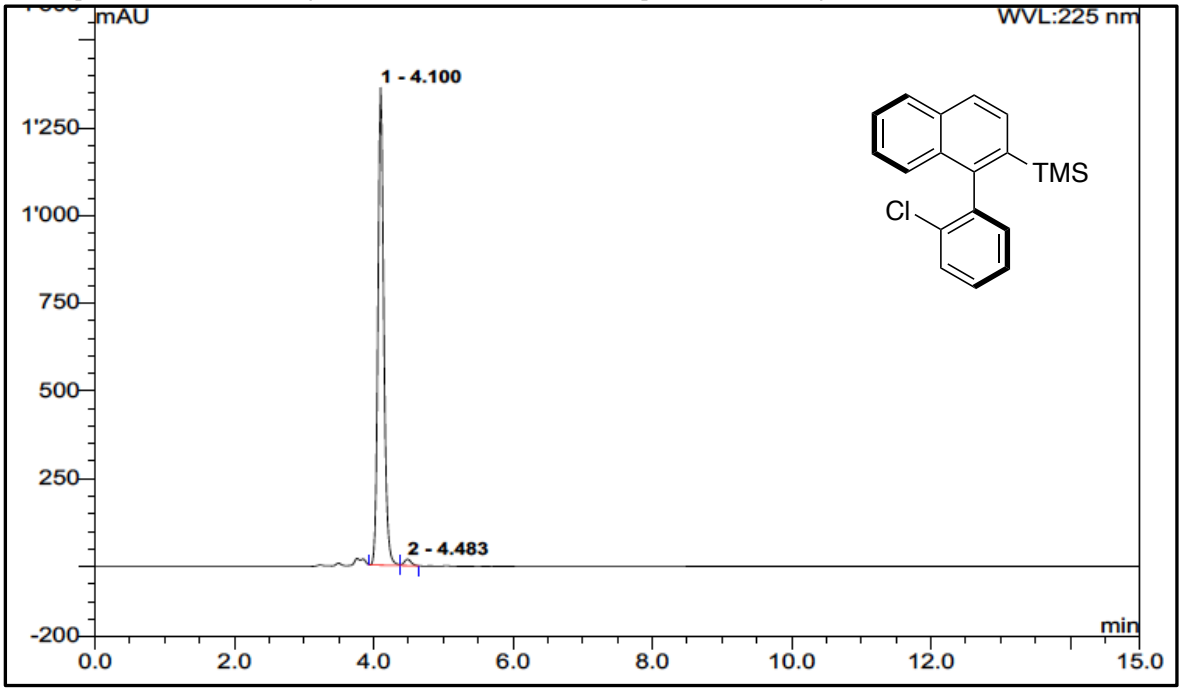


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5.65	n.a.		88.589	12.079	3.21	n.a.	BMB*
2	7.62	n.a.		1648.483	363.724	96.79	n.a.	BMB*
Total:				1737.072	375.803	100.00	0.000	

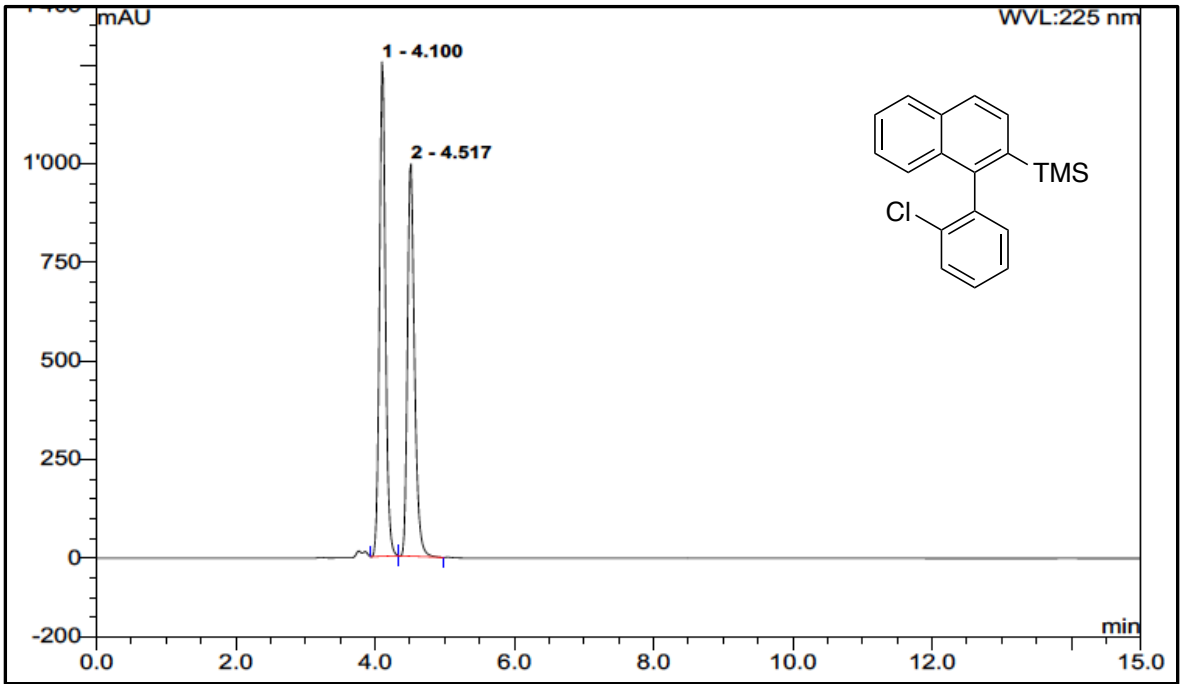


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5.63	n.a.		1686.384	234.487	50.01	n.a.	BMB*
2	7.62	n.a.		1083.537	234.382	49.99	n.a.	BMB*
Total:				2769.921	468.869	100.00	0.000	

Chiralpak AD-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

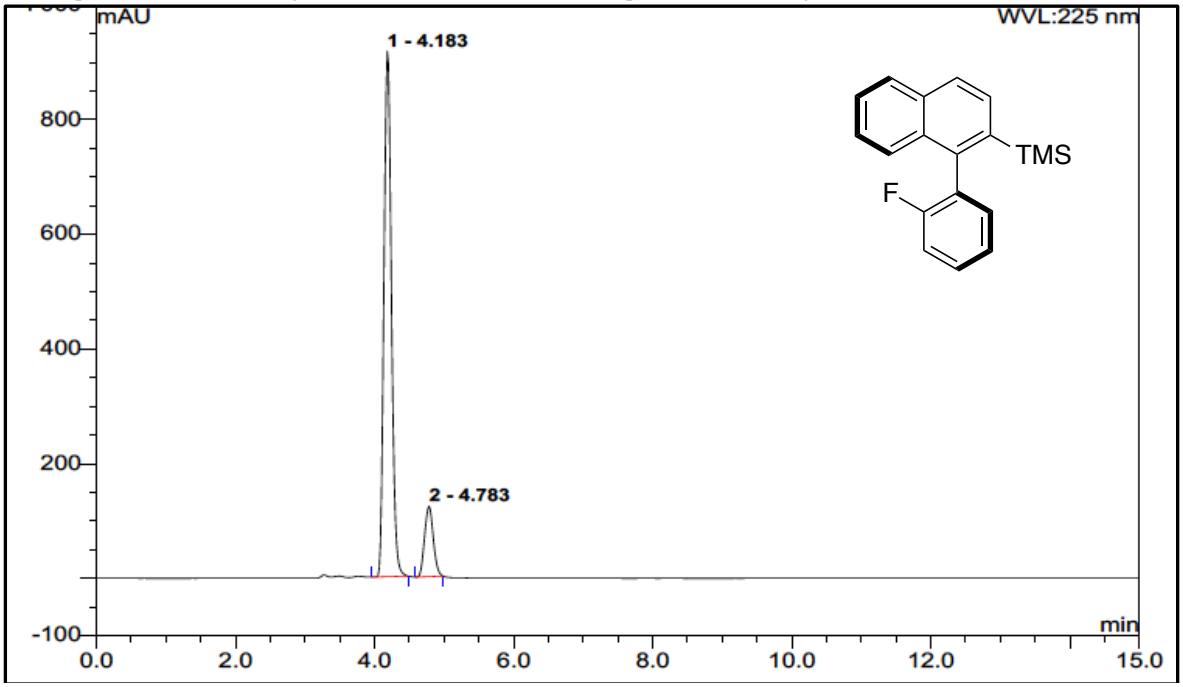


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	4.10	n.a.		1361.102	132.961	98.43	n.a.	BM *
2	4.48	n.a.		18.459	2.121	1.57	n.a.	MB*
Total:				1379.561	135.082	100.00	0.000	

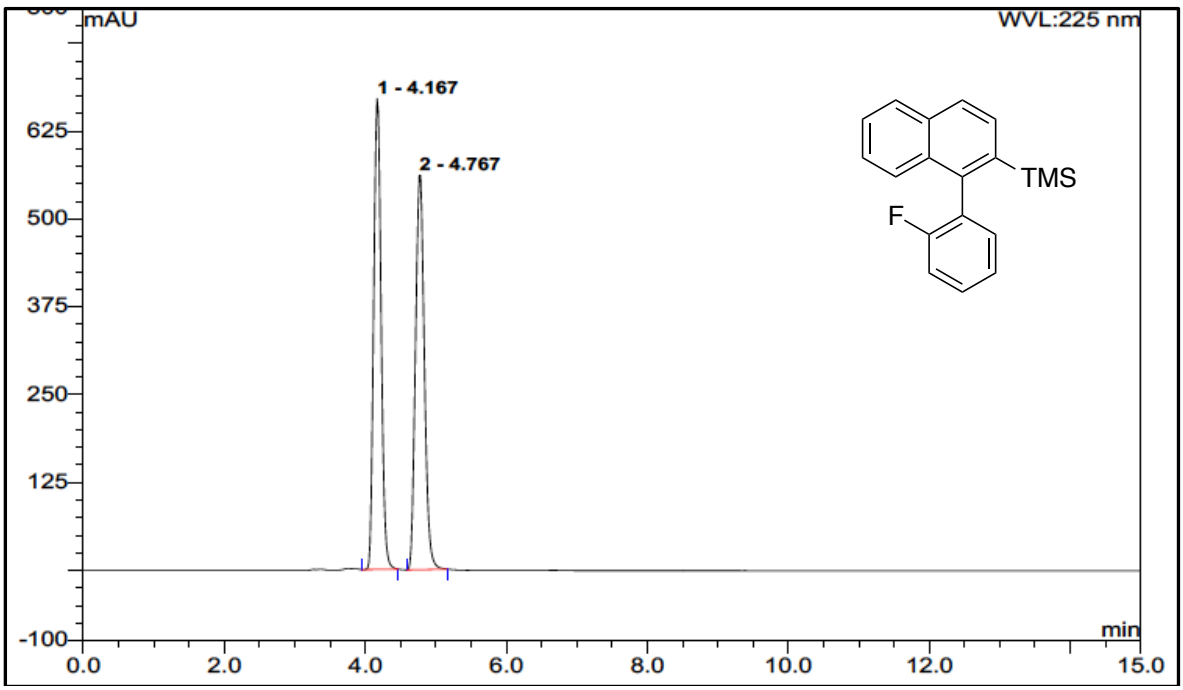


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	4.10	n.a.		1253.376	125.584	51.80	n.a.	BMb*
2	4.52	n.a.		994.762	116.851	48.20	n.a.	bMB*
Total:				2248.138	242.436	100.00	0.000	

Chiralpak IC-3 column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

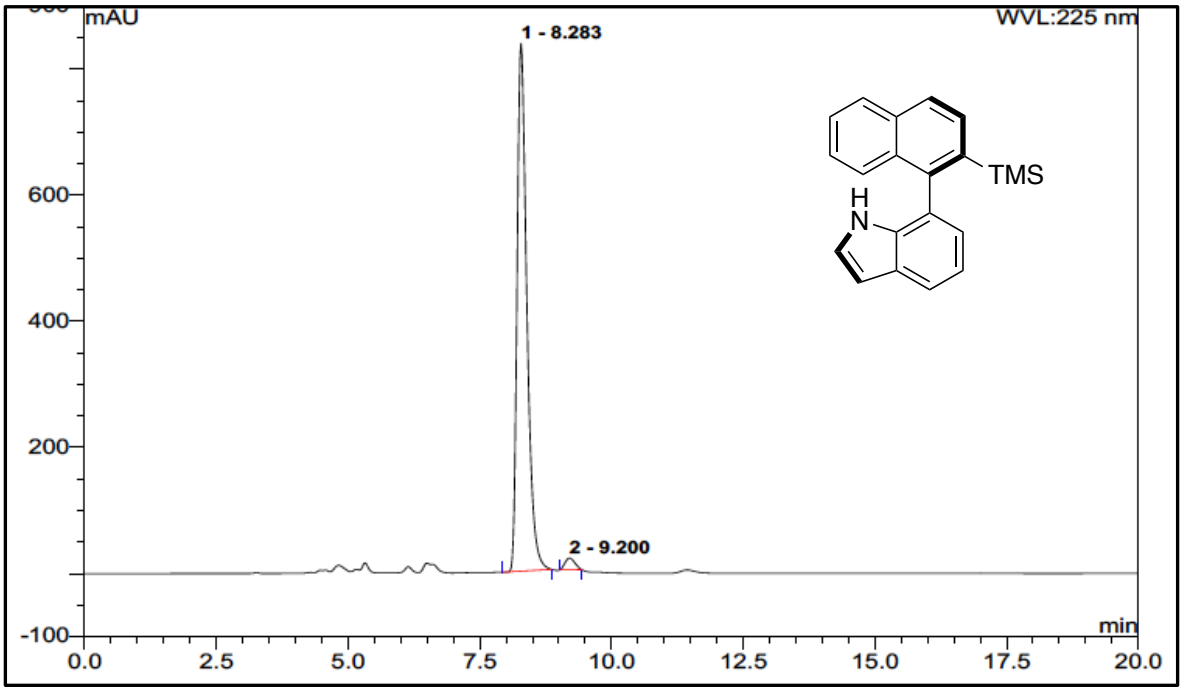


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	4.18	n.a.		916.488	114.903	86.67	n.a.	BMB*
2	4.78	n.a.		122.871	17.673	13.33	n.a.	BMB*
Total:				1039.358	132.576	100.00	0.000	

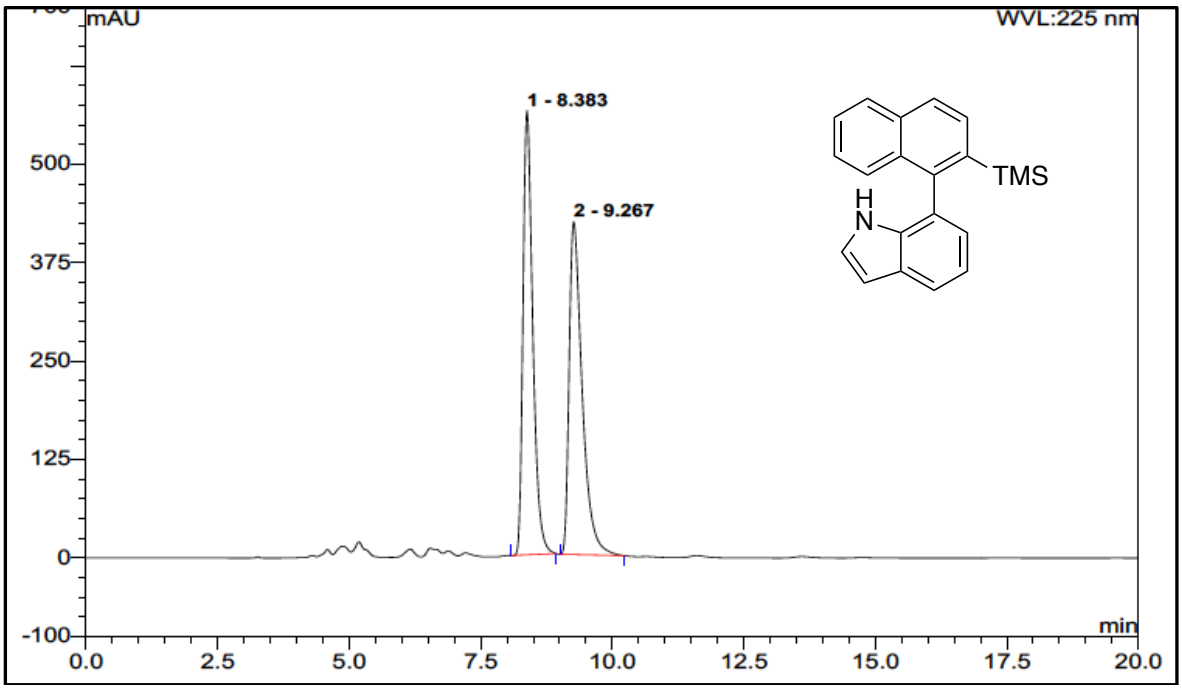


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	4.17	n.a.		670.002	81.623	49.93	n.a.	BMB*
2	4.77	n.a.		561.233	81.843	50.07	n.a.	BMB*
Total:				1231.236	163.466	100.00	0.000	

Chiralpak IA column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

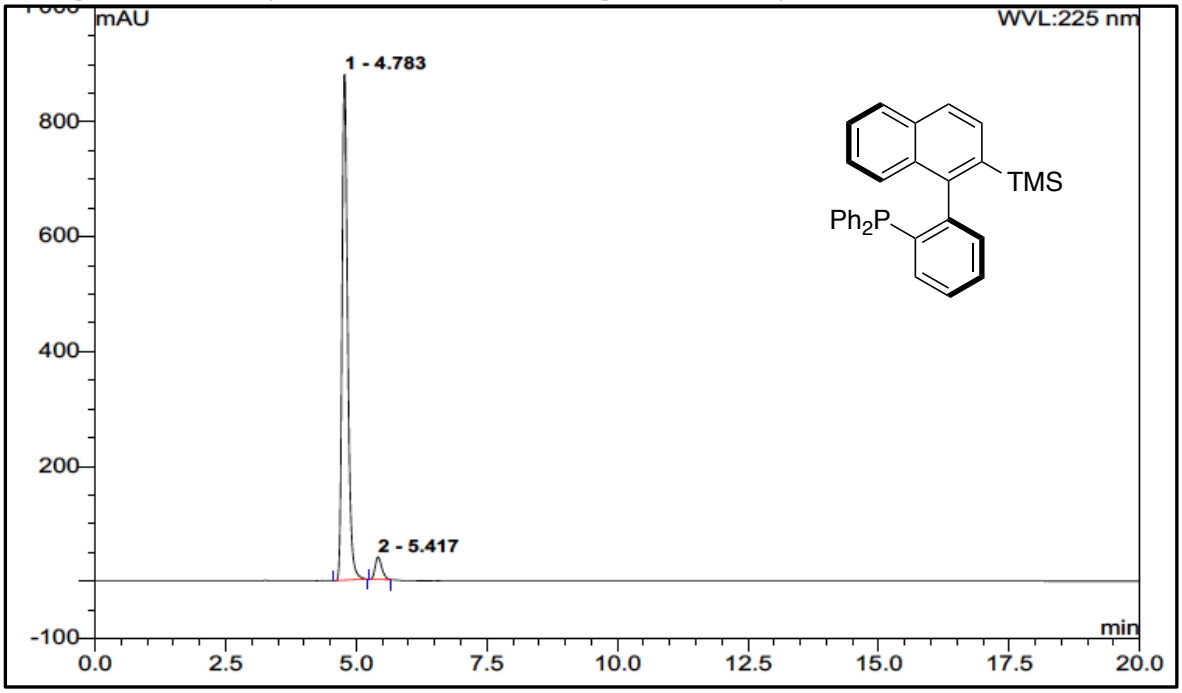


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	8.28	n.a.		836.788	179.105	97.81	n.a.	BMB*
2	9.20	n.a.		18.633	4.017	2.19	n.a.	BMB*
Total:				855.421	183.122	100.00	0.000	

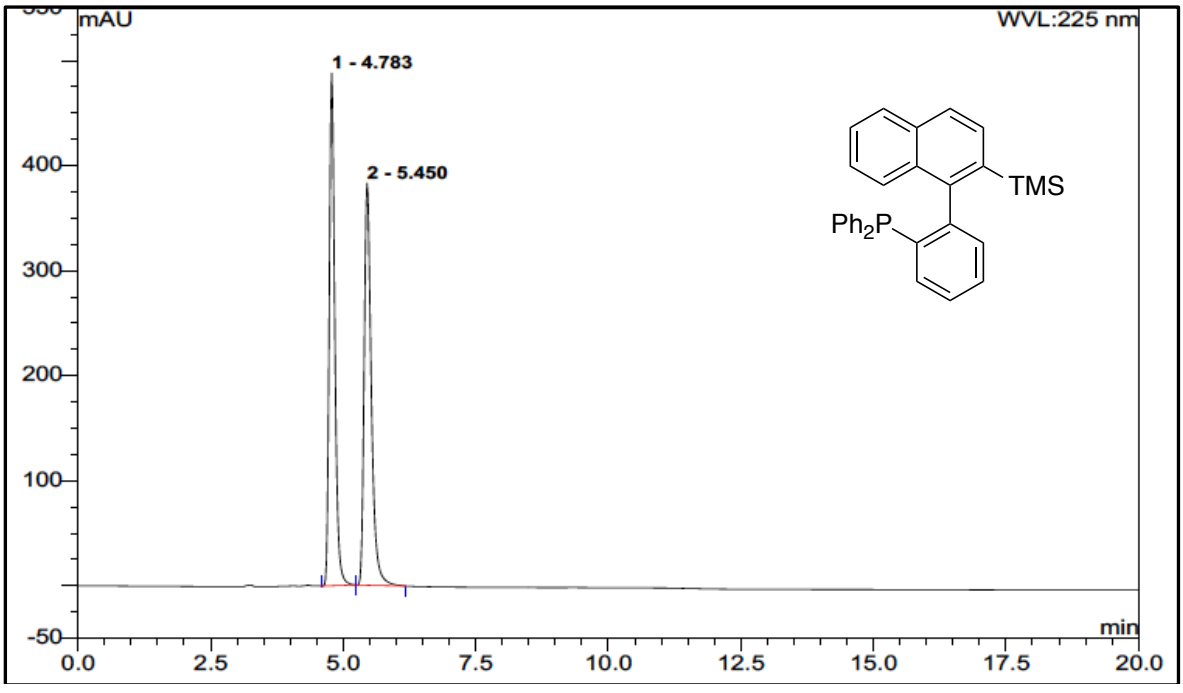


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	8.38	n.a.		564.431	121.306	50.07	n.a.	BMB*
2	9.27	n.a.		422.862	120.968	49.93	n.a.	BMB*
Total:				987.293	242.274	100.00	0.000	

Chiralpak IA column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

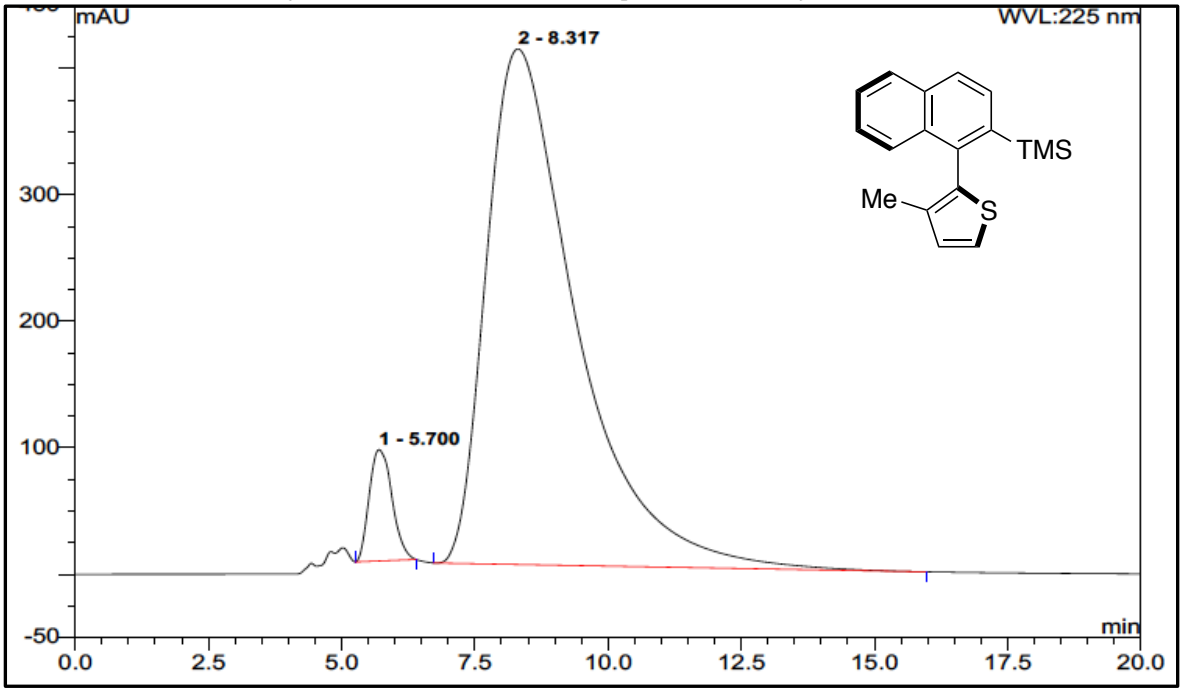


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	4.78	n.a.		881.236	109.702	94.96	n.a.	BMB*
2	5.42	n.a.		39.627	5.822	5.04	n.a.	BMB*
Total:				920.864	115.523	100.00	0.000	

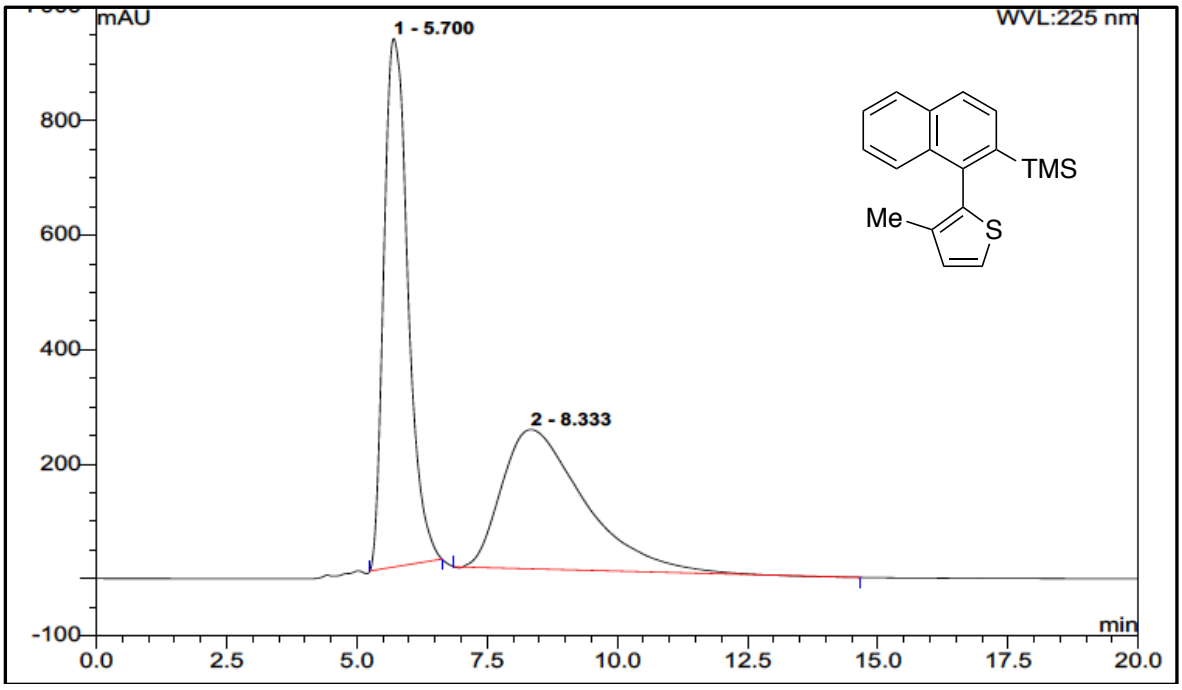


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	4.78	n.a.		487.862	59.607	49.87	n.a.	BMB*
2	5.45	n.a.		382.715	59.910	50.13	n.a.	BMB*
Total:				870.577	119.517	100.00	0.000	

Chiralcel OJ-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)

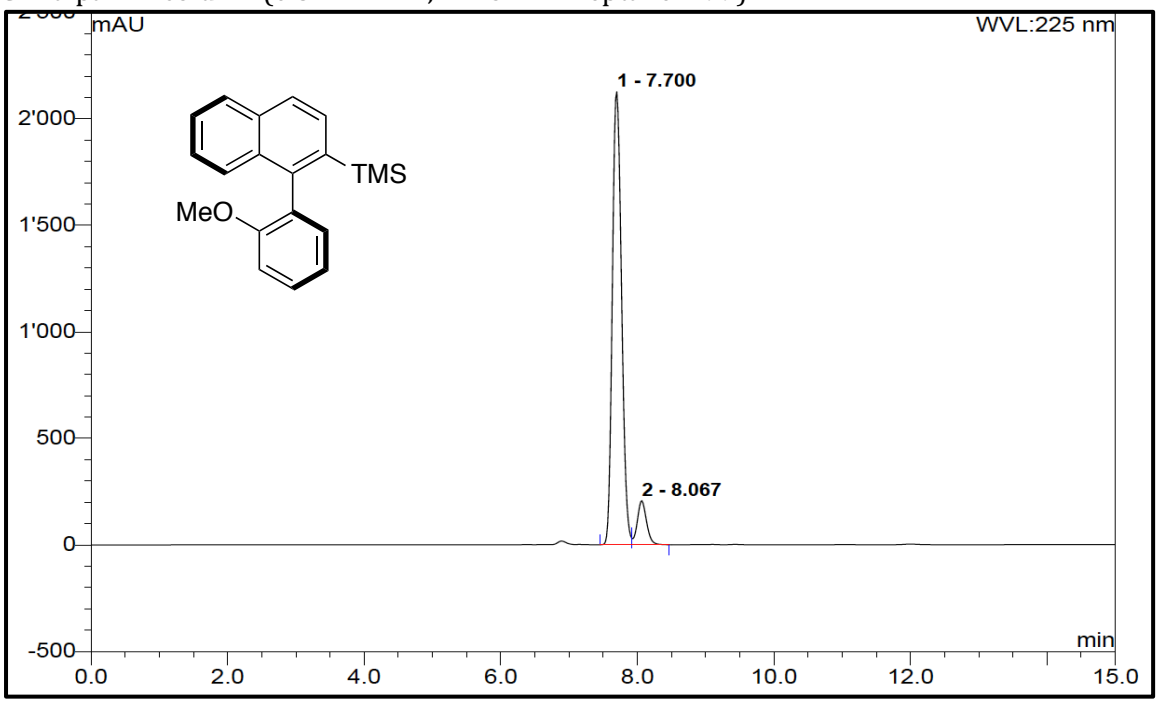


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5.70	n.a.		88.020	43.810	5.20	n.a.	BMB*
2	8.32	n.a.		407.591	798.660	94.80	n.a.	BMB*
Total:				495.611	842.470	100.00	0.000	

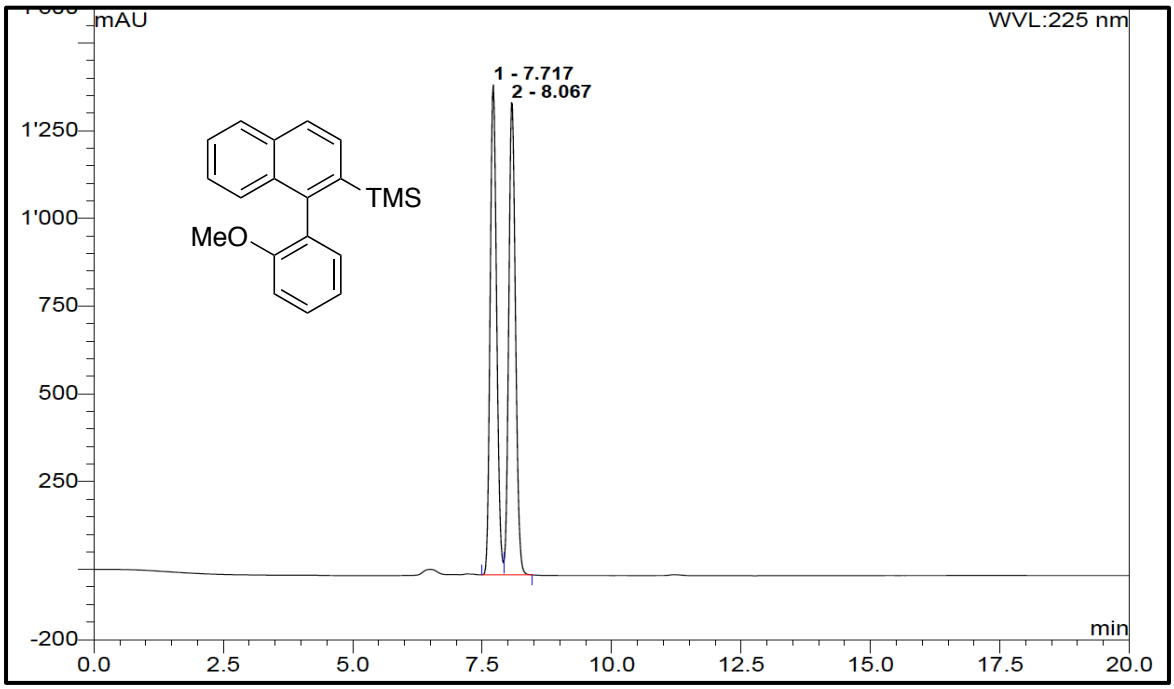


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	5.70	n.a.		923.612	495.610	52.58	n.a.	BMB*
2	8.33	n.a.		243.319	446.944	47.42	n.a.	BMB*
Total:				1166.931	942.555	100.00	0.000	

Chiralpak IA column (0.5 mLmin^{-1}, *i*-PrOH : *n*-heptane 1:99)

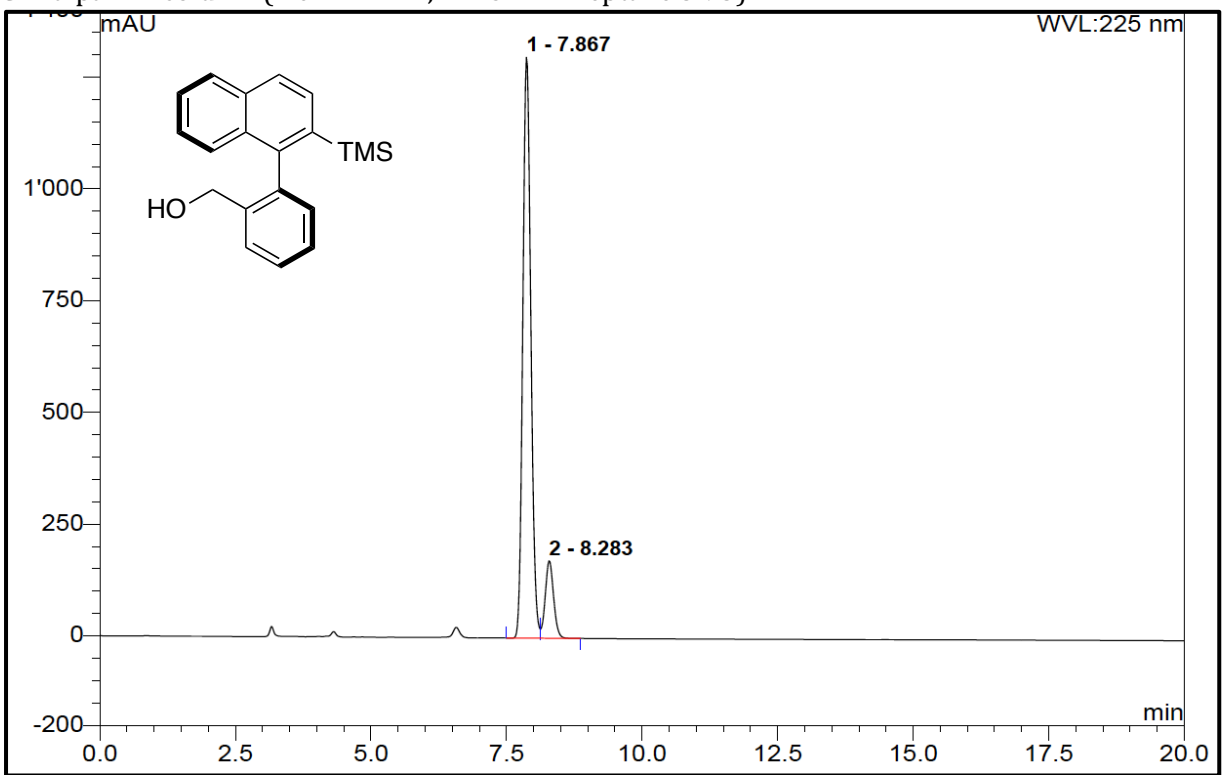


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.70	n.a.		2126.461	332.146	91.09	n.a.	BM *
2	8.07	n.a.		206.119	32.469	8.91	n.a.	MB*
Total:				2332.580	364.615	100.00	0.000	



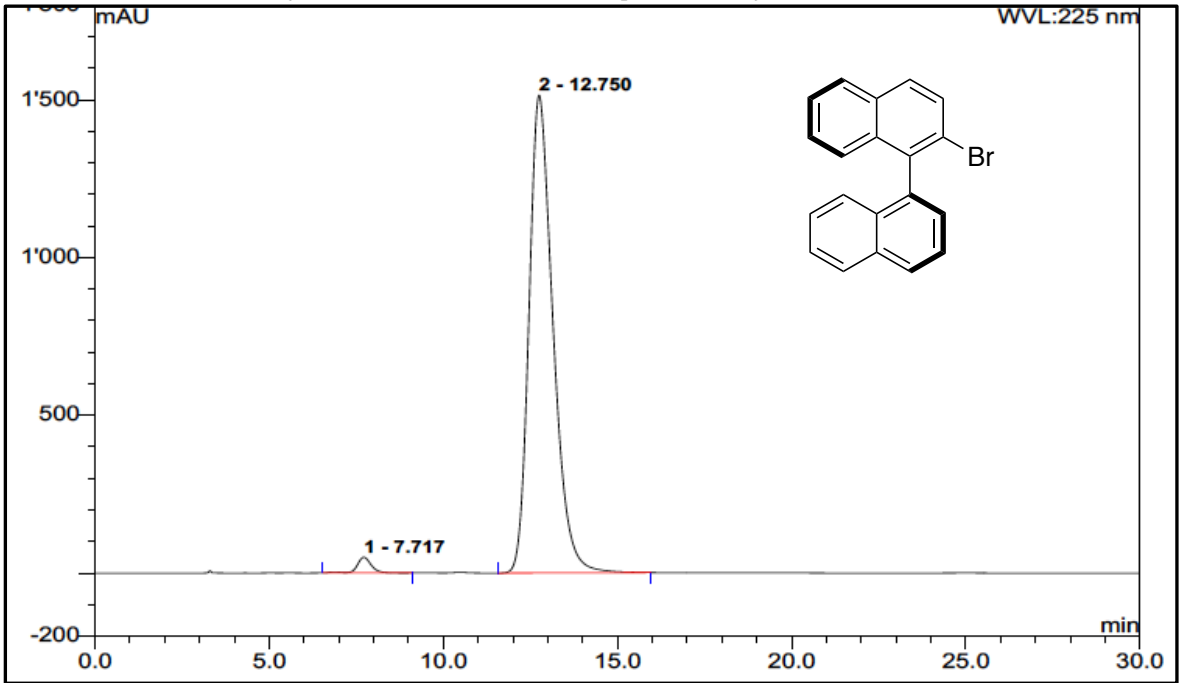
No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.72	n.a.		1396.510	203.643	49.82	n.a.	BM *
2	8.07	n.a.		1345.808	205.082	50.18	n.a.	MB*
Total:				2742.319	408.725	100.00	0.000	

Chiralpak IA column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 5:95)

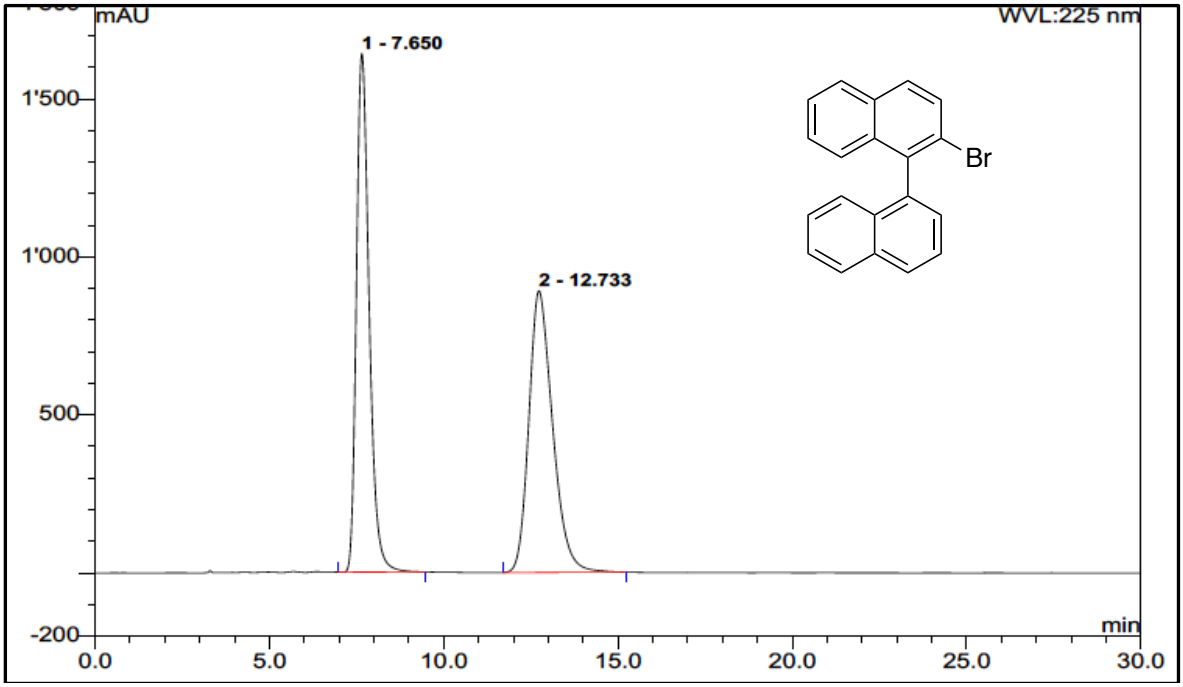


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.87	n.a.		1299.699	222.260	87.65	n.a.	BM *
2	8.28	n.a.		173.401	31.318	12.35	n.a.	MB*
Total:				1473.100	253.578	100.00	0.000	

Chiralcel OJ-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 5:95)

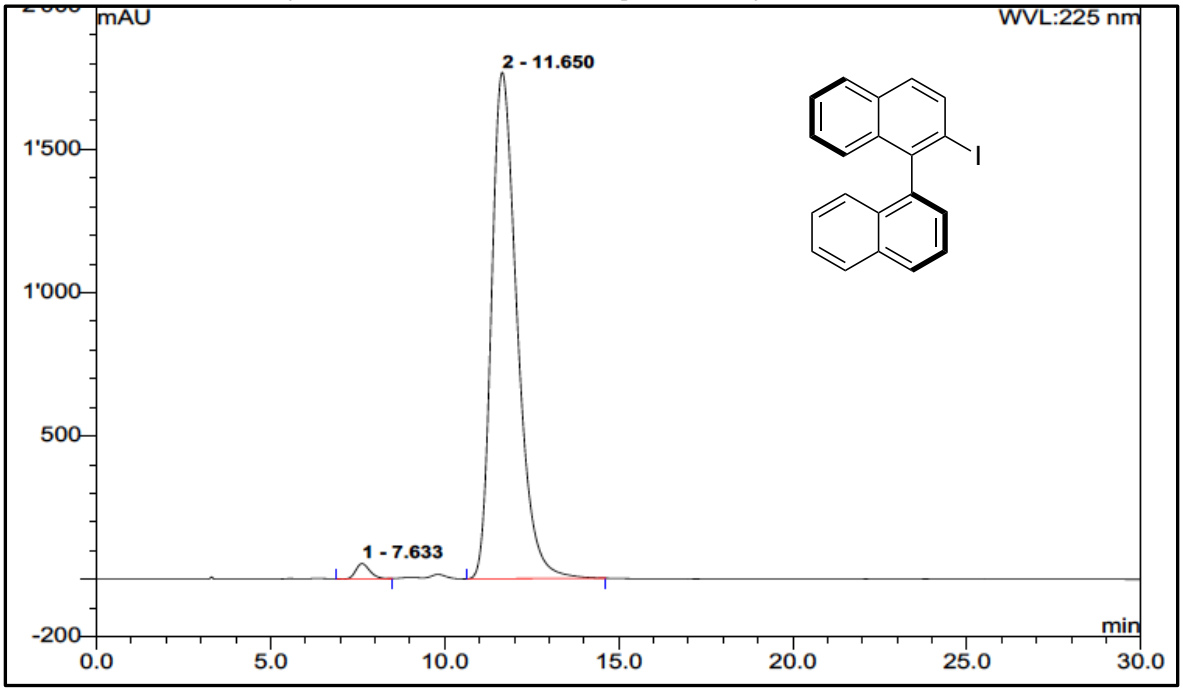


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.72	n.a.		49.611	23.164	1.88	n.a.	BMB*
2	12.75	n.a.		1513.981	1208.637	98.12	n.a.	BMB*
Total:				1563.592	1231.801	100.00	0.000	

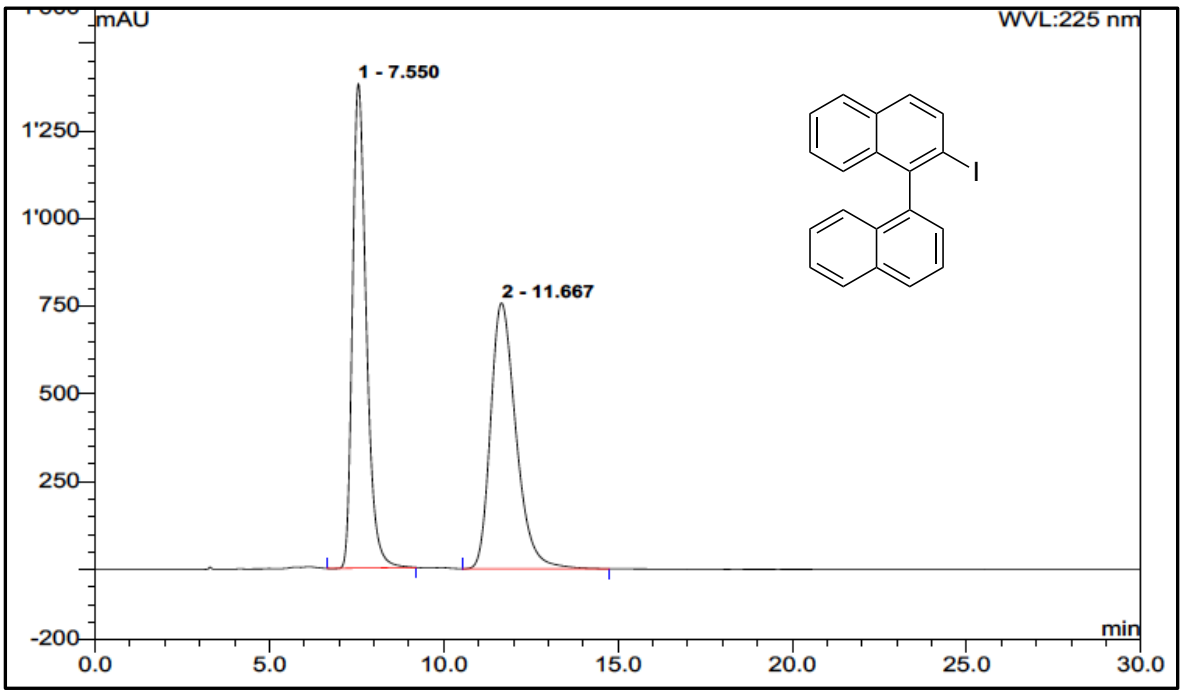


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.65	n.a.		1641.083	694.695	49.68	n.a.	BMB*
2	12.73	n.a.		891.221	703.780	50.32	n.a.	BMB*
Total:				2532.304	1398.475	100.00	0.000	

Chiralcel OJ-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 5:95)

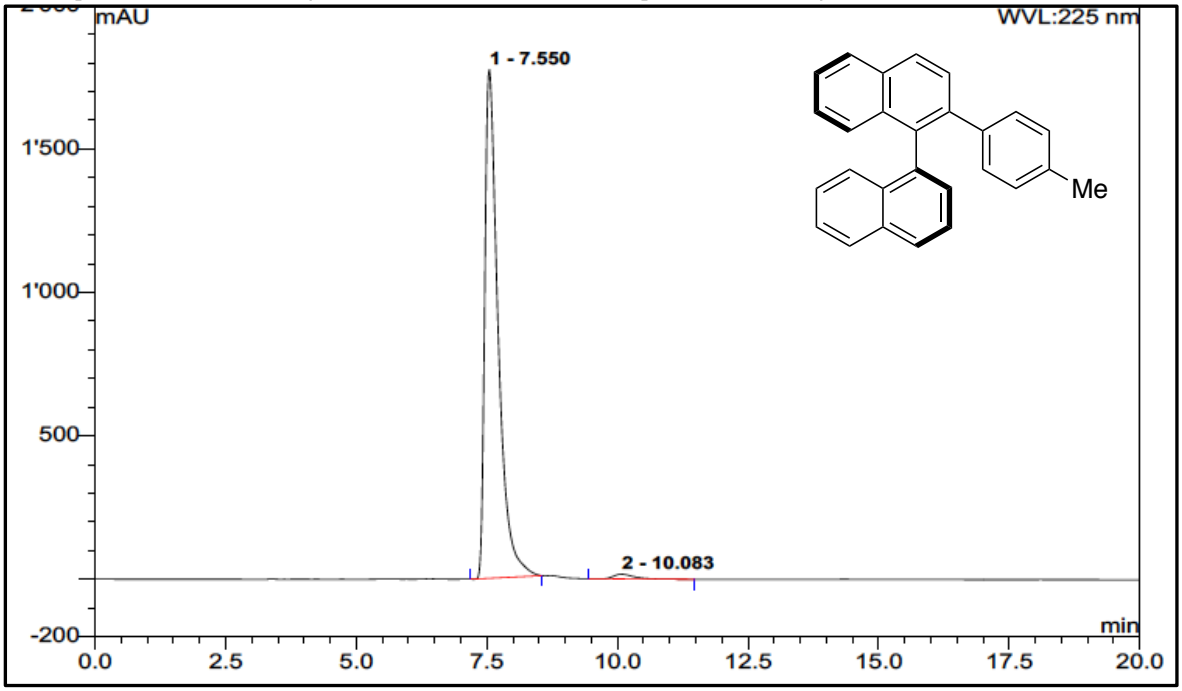


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.63	n.a.		52.810	24.314	1.59	n.a.	BMB*
2	11.65	n.a.		1766.779	1500.310	98.41	n.a.	BMB*
Total:				1819.589	1524.624	100.00	0.000	

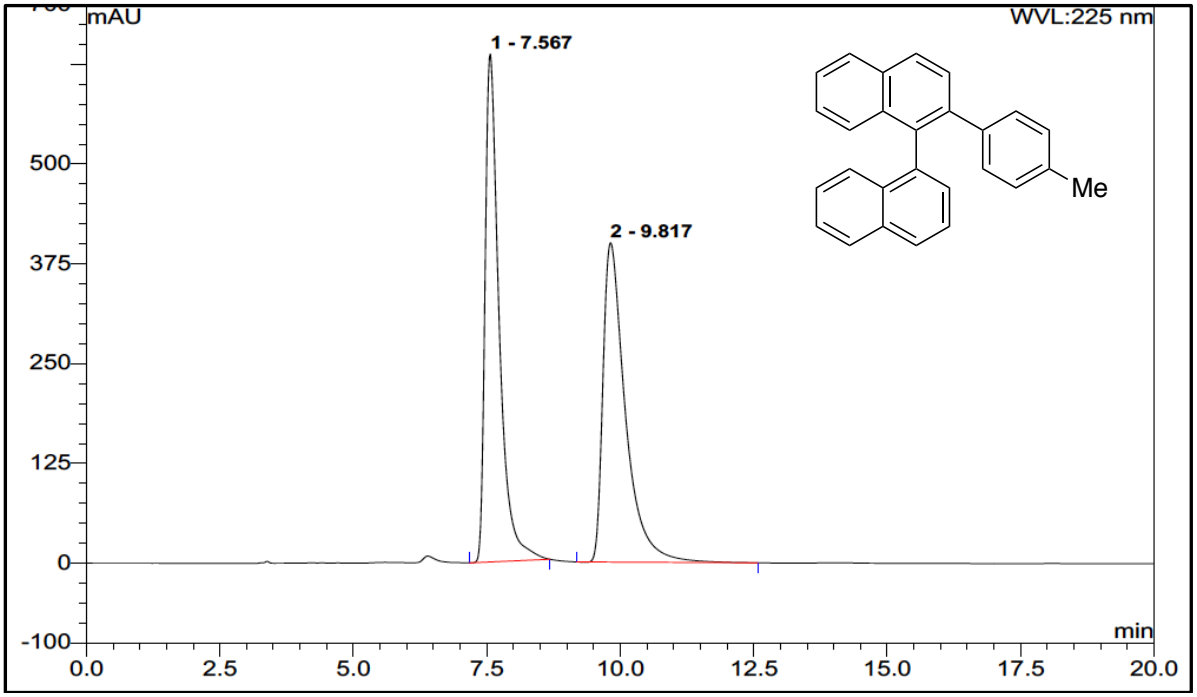


No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.55	n.a.		1381.097	635.744	49.80	n.a.	BMB*
2	11.67	n.a.		757.497	640.922	50.20	n.a.	BMB*
Total:				2138.594	1276.666	100.00	0.000	

Chiralpak AD-H column (1.0 mLmin^{-1}, *i*-PrOH : *n*-heptane 0.2:99.8)



No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.55	n.a.		1773.336	525.997	98.63	n.a.	BMB*
2	10.08	n.a.		16.451	7.284	1.37	n.a.	BMB*
Total:				1789.787	533.281	100.00	0.000	



No.	Ret.Time min		Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount n.a.	Type
1	7.57	n.a.		636.452	194.608	50.00	n.a.	BMB*
2	9.82	n.a.		400.126	194.633	50.00	n.a.	BMB*
Total:				1036.578	389.240	100.00	0.000	

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6 Appendix

6.1 Acknowledgments

First and foremost I would like to express my deepest gratitude to my mentor *Prof. Dr. Christof Sparr* for the last 5 years. Starting as his first Master and PhD student, accompanying the evolvement of his research and group, learning from his knowledge, following his creativity and passion as well as his structured way of thinking is a rewarding experience. I could profit a lot, scientifically but probably even more important personally. I thank for guidance and the sometimes needed refocussing to the essential core tasks when getting lost in details, but also for the freedom that allowed me to explore novel ideas in "Friday evening"-experiments, also throughout the week. Thank you *Christof*, for this opportunity and the confidence in me.

I thank *Prof. Dr. Marcel Mayor* not only for co-examining my PhD thesis, but also for an inspirational lecture during my master studies. This lecture changed my view of organic synthesis and since then I understand it as dirigible playground to access functional molecular structures.

I am thankful to *Prof. Dr. Karl Gademann* for inspiring speeches, teaching and supporting the Sparr group while in Basel.

I want to thank, the University of Basel for financial support, the *Camille and Henry Dreyfus-Fond* for a stipend and the *Swiss Chemical Society* for a "Chemistry Travel Award" and a "Poster Presentation Prize".

I am deeply grateful to my former mentor *Dr. Mark Kantor* for my apprenticeship at RCA in Freiburg. He taught me everything about organizing work and analytical chemistry. Another thank you to my colleagues *Thorsten Huber* and *Jens Bucher*.

Very special thanks go to my colleagues and friends *Christian Fischer*, *Vincent Fäseke*, *Dominik Lotter*, *Reto Witzig*, *Bouthayna Zilate*, *Alessandro Castrogiovanni*,

Felix Raps, *Dominik Scherrer* and *Zlatko Joncev*. We had a great time together and I always enjoyed to be a member of such a dedicated research team. Especially I like to thank Christian, Reto and Dominik for proof-reading this thesis.

I want to express my gratitude to the members of the Gademann Group I had the luck to work with. *Regina Berg*, *Hideki Miyatake* and *Erika Crane* for their wisdom and especially my Lab mates *Samuel Bader*, *Manuel Scherer* and *Christophe Daeppen* for welcoming me in their laboratory and creating a great atmosphere.

I like to thank my practicum students Fadri Chistoffel, Laurent Jucker and Markus Jakobi for their skillful work and their interest in exploring new research directions.

Many thanks to *PD Dr. Daniel Häussinger* and his NMR-team for the great service, to *Dr. Markus Neuburger* for X-ray crystallography and *Dr. Heinz Nadig* for HR-MS measurements. Furthermore, I like to thank the "Werkstatt-Team" for technical support and all other people keeping the Chemistry Department alive and running.

Ich bedanke mich bei meinen Freunden *Andreas Faller*, *Ralf Eydner*, *Johannes Widmaier* und *Dennis Reimann* für die schöne Zeit abseits der Chemie.

Besonders danke ich meinen Eltern für die Untersützung, das entgegengebrachte Vertrauen und die Möglichkeit eine Universität besuchen zu dürfen. Meinem Bruder *Lukas* danke ich für die abwechslungsreichen Bau- und Holzfäller-Tätigkeiten, seinen Rat und seiner Frau Ruth und Tochter Valentina für die gemeinsamen Stunden.

Meiner Freundin *Franziska* danke ich für ihre Liebe und die schönen gemeinsamen Jahre.

6.2 Curriculum Vitae

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Academic Education

05/2018 –	**Massachusetts Institute of Technology** Postdoctoral Fellow in Synthetic Organic Chemistry Advisor: Prof. Dr. Stephen L. Buchwald
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09/2013 – 03/2014	**University of Basel** MSc in Chemistry Advisor: Prof. Dr. Christof Sparr
07/2013 – 08/2014	**University of Basel** MSc Internship Advisor: Prof. Dr. Andreas Pfaltz
09/2009 – 10/2012	**University of Freiburg** BSc in Chemistry Advisor: Prof. Dr. Bernhard Breit

Employment History

04/2014 – 04/2018	**University of Basel** Research Assistant: PhD candidate in Synthetic Organic Chemistry. Advisor: Prof. Dr. Christof Sparr
09/2006 – 09/2009	**Chemical Laboratory Assistant in Industry.** Responsible for process analysis: HPLC, GC, UV-VIS, FT-IR. Reuter Chemischer Apparatebau (RCA) in Freiburg, Germany. Advisor: Dr. Marc Kantor

Approved Research Projects

05/2018 –	**Postdoc with an Early Postdoc.Mobility fellowship** of the Swiss National Science Foundation. Investigation of Intermediary Copper-Hydride Complexes. Buchwald Research Group, MIT in ÍCambridge, USA.

04/2014 – 04/2018	**PhD in Chemistry.** Direct transformation of carboxylic acid esters into arenes. Sparr Research Group, University of Basel.
09/2013 – 03/2014	**Master Thesis.** Development of an organocatalytic atroposelective aldol condensation reaction. Sparr Research Group, University of Basel.
07/2013 – 08/2014	**MSc Internship.** Synthesis of Ir-catalysts and investigation of catalytic asymmetric hydrogenation. Pfaltz Research Group, University of Basel.
09/2009 – 10/2012	**BSc in Chemistry.** Synthesis of tricyclic ketone derivatives *via* an intramolecular Rh-catalyzed hydroacylation. Breit Research Group, University of Freiburg, Germany.

Memberships in Scientific Societies

08/2015 – present	Member of the **Swiss Chemical Society**.

Conferences/Prizes/Awards

05/2017	**Early Postdoc.Mobility fellowship** of the Swiss National Science Foundation. Start date Postdoc: 05/2018 at MIT, Cambridge, USA.
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02/2017	**Camille and Henry Dreyfus Stipendium**, University of Basel.
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08/2016	Selected for the **BASF International Summer Course 2016** in Ludwigshafen.
07/2016	Poster Presentation at the **Belgian Organic Synthesis Symposium BOSS 2016** in Antwerp.
09/2015	**Speaker** at the **SCS Fall Meeting** in Lausanne.

Publications in peer-reviewed scientific journals

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